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BRITISH MEDICAL JOURNAL

LONDON SATURDAY AUGUST 7 1948

ANTIHISTAMINE SUBSTANCES*

BY

Sir HENRY DALE, O.M., G.B.E., F.R.C.P., F.R.S.

As one of those who took part in the recognition of histamine in nature and in the first detailed examination of its intense physiological activities, I shall try to avoid the temptation to be unduly reminiscent. I may just remind you that at that time, nearly 40 years ago, much interest in circles concerned with experimental pathology was centred on the syndrome of the anaphylactic reaction and on the curious differences which it presented in the different species. You can imagine that Laidlaw and I (Dale and Laidlaw, 1910, 1911) had to discipline our eagerness as we examined one by one the actions of histamine on the different organs and systems of the dog and the guinea-pig in particular, and found them fitting neatly, like units of a jigsaw puzzle, into the contrasting pictures of the anaphylactic reactions in those two species as others had then recently described them. Biedl and Kraus (1910) had already drawn attention to the close correspondence—even closer, in fact—between the contrasted reactions of the normal dog and guinea-pig to intravenous Witte's peptone and those of the anaphylactic dog and guinea-pig to the reinjection of the antigen. I well remember Biedl's account of this at the International Physiological Congress in Vienna in 1910; and my own decription later in the same programme of the newly discovered and, except for a few points, identical effects of histamine on the same two species. There was, of course, an obvious probability that a correspondence at so many points would have some significance, but it was difficult to guess just what it might mean. It certainly did not mean, what some were too ready to assume, that histamine was the hypothetical "anaphylatoxin" of which there was then so much talk, as a poison supposed to be liberated in the blood by some kind of enzymatic cleavage of the reinjected antigen; for there were features of the anaphylactic and peptone shocks which were not represented in the actions of histamine, such as the gross swelling of the liver and the failure of the shed blood to clot, and Laidlaw and I thought, and said, that these gaps must be taken into account in any discussion of the meaning of the general correspondence.

That, of course, is ancient history, and a great deal has happened since to clarify what was then obscure. Fortunately there have been several most valuable reviews of the all too abundant literature. I may mention the monograph of Feldberg and Schilf in 1930, Gaddum's (1936) monograph on vasodilator substances, and quite recently a review-lecture by Gaddum (1948), full of suggestive thought, dealing chiefly with later and contemporary work. Let me just indicate what seem to me a few of the landmarks of progress on the way to the present position, and then mention certain outstanding problems which seem to be worth further attention, if only to provide us with a more completely rational basis for the use of the so-called antihistamines with which to-day's discussion is largely concerned.

*Read in opening a discussion in the Section of Pharmacology at the Annual Meeting of the British Medical Association, Cambridge, 1948.

Landmarks of Progress

First, as to the pharmacological action of histamine, I suppose that we shall now agree that it is a general stimulator of the tone and rhythm of plain muscle in most mammalian species, the *Muridae* presenting an exception; and then that the vasodilator-depressor action which it produces so conspicuously on intravenous injection into certain species, including the human, is due to a special inhibitor action on the tone of minute blood vessels, involving always the tone of the capillaries and extending in some species, man among them, but to different levels in the different species, on to the ultimate arteriolar branchings. The involvement of the capillaries, and the resulting permeability of their walls if the action is powerful, came to light when Laidlaw, Richards, and I resumed the study of the action of histamine in the middle of the first world war under the stimulus of the demand for any light which experimental work could throw, even obliquely, on the obscure problems of wound shock, a demand which was naturally revived in the second world war. Concerning our work (Dale and Richards, 1918; Dale and Laidlaw, 1918) in 1917–18, I should just like to note, in passing, the useful and stimulating coincidence with our conclusions at that juncture of those reached by others who were then working on similar reactions. Krogh (1929), as we learned a little later, was already engaged on his more general study of the variable tone of the capillary vessels; Lewis, Cotton, and Slade (1917) had already published a year earlier the initial stage of what became Lewis's classical studies of the "threefold reaction" of the small blood vessels of the human skin to various injuries; and, still more aptly for our immediate purpose, Sollmann and Pilcher (1917) had just shown that application of histamine itself in high dilutions to the human epidermis after microscopic breaches of its surface caused local capillary dilatation and weal formation. We ourselves, being impressed by the analogy, pointed out that a not too destructive local injury, such as a blow from a whip or cane, would produce a closely similar local vascular effect, just as the generalized effects of histamine on the blood vessels which we were describing resembled those of a generalized tissue injury.

What was known of the pharmacological actions of histamine was thus already sufficient to arouse a suspicion that its release in response to injury of tissue cells *might* account for a substantial part at least of the resulting vascular and other reactions, whether the injury was produced by mechanical trauma, by corrosive or precipitant

chemicals, or, in an anaphylactic subject, by the specific antigen. For by that time I think it was generally agreed that the anaphylactic condition was due, at least in the main, to the predominant attachment of a precipitating immune substance to the tissue cells, and that the different symptomatology of the shock in different species was due to the way in which this sensitizing antibody was allocated among the cells of the different organs—being mainly attached to those of the liver of the dog, and mainly to those of plain muscle in the guinea-pig. We were not yet entitled, however, to indulge in any definite theories about such a release of histamine, since we had no real evidence so far that it was a constituent of normal tissue cells; we had only the early finding of it by Barger and myself (1911) as a constituent of intestinal mucosa, which we could hardly regard as a typical tissue for this purpose. Most of a further decade was required, then, before the evidence from different sources once again converged to a new point of advance. We had the resumption of the brilliant series of experiments, chiefly on human skin, by Lewis and his team, producing cumulative evidence of the release by the various kinds of mild injury of something having all the observable properties of histamine, but always by them called "H-substance" with a truly scientific caution. I think there can be little reason to doubt that they were dealing with histamine itself, either free or in loose association with some more complex vector.

I suppose that everybody working with this group of phenomena had in mind the possibility that the effect of the specific antigen on the cells of the anaphylactic animal might be to cause histamine to appear. I, rather perversely perhaps, had myself been inclined (Dale, 1919) for a time to discount it, pointing out that for aught we knew the action of histamine itself might be to produce an aggregating effect comparable to that which we had reason to impute to the reaction between anaphylactic antigen and cell-fixed antibody. Abel and Kubota (1919) had favoured the idea that histamine was somehow concerned, but I believe that it was Lewis (1927) who, having seen a dermal allergic reaction and recognized the characteristic "threefold response," first definitely attributed the effect to the appearance of histamine, or, more strictly, "H-substance." It was at this point, however, that there was once again such a convergence of researches; for at that same period an irrelevant side issue had led me to organize with Best, Dudley, and Thorpe (1927) an effort to obtain unequivocal evidence regarding the nature of the substances with histamine-like actions extractable from different fresh tissues—liver first, then lung, then muscle, then spleen. In all cases it was histamine itself, detachable without any drastic treatment from more complex materials, its tendency to cling to which had apparently misled earlier workers. So that it did not seem necessary to suppose, as Abel and even Lewis had been inclined to do, that histamine was *formed* in response to injurious stimuli, including that of the anaphylactic antigen, or allergic haptene; it was there already, held inside the cell in inactive association, and we had only to postulate its release. And then that chapter seemed to be rounded off and completed when Dragstedt and his associates found histamine in the lymph flowing from the dog's liver in the anaphylactic shock (Gebauer-Fuelnegg, Dragstedt, and Mullenix, 1932), and Feldberg with his team found it appearing in the effluent from the perfused lungs of an anaphylactic guinea-pig (Bartosch, Feldberg, and Nagel, 1932) when the antigen was added to the inflowing saline solution and evoked the bronchial constriction.

All this evidence, of course, left it not only possible but practically certain that active and normally intracellular constituents other than histamine would also be liberated with it. We know now, for example, that heparin is liberated from the liver by peptone or the anaphylactic reaction to make the blood incoagulable. Histamine, however, is by a long way the most potent in pharmacological action of any such cell constituents as are known, and it is the one which particularly concerns the present discussion. Let us consider, then, some points concerning the manner of its release which bear on our problem, and others on which more evidence would be of value.

Mode of Histamine Release

1. Consider the relationship between the cells from which histamine is released—the sensitized cells on which the antigen or haptene acts in the case of the allergic reactions—and those which react to the released histamine, producing the familiar syndrome. The cells which release histamine and those which respond to it may be identical, as they probably are when sensitized plain muscle encounters the antigen, and we may plausibly picture this as a reaction to histamine internally liberated and speak of it as a response to *intrinsic* histamine. On the other hand, when histamine is released in the liver it is obviously carried widely by the circulation to other histamine-sensitive tissues, causing a general vasomotor collapse and stimulating the plain muscle of remote organs. Even when the injury releases histamine from epidermis or nasopharyngeal epithelium it is not the epithelial cells which respond to it but the subjacent vascular plexus, which thus reacts to *extrinsic* histamine. It will be clear that the antagonism of an antihistamine, whatever the precise mechanism of its action, may be widely different against histamine from within and histamine from without. There might obviously be analogies with the action of atropine in suppressing readily certain effects of acetylcholine applied from without while leaving practically unchanged corresponding effects of its release from nerve endings. There is an even closer analogy in Schild's observation that the guinea-pig's sensitized plain muscle can be made tolerant of excess of histamine in the surrounding fluid so that it gives no response to further additions of histamine to the bath but still responds to the specific antigen—presumably, therefore, to *intrinsic* histamine. Such considerations may throw light on the relative effectiveness of antihistamines in urticaria and vasomotor rhinitis on the one hand and in spasmodic asthma on the other. The point is at least worth discussion in the light of clinical experience of the relative values of these drugs in different types of allergic reaction.

2. I think that we need more evidence yet concerning the manner of the release of histamine which might furnish more details to show whether, when so liberated, it is in free solution or associated with larger molecules as an "H-substance." Even if we accept the view that disturbance of the colloidal dispersion of the protoplasm liberates the histamine we still need more evidence whether it does so directly or by setting in action some enzyme system to which the actual liberation of histamine is due. Rocha e Silva's evidence that pure trypsin has this action is highly suggestive (Rocha e Silva and Andrade, 1945; Rocha e Silva, 1946), as are the earlier observations of Feldberg and Kellaway (1938) on the special factors concerned in the generally similar effects of cobra and bee venom. Kellaway's recent lecture (1947) gives a valuable review. We ought to know more, too, about the apparent new formation of "histamine" in scalded mice as recorded by Dekanski (1945).

3. We need still more information about the form in which histamine circulates in the blood. Estimates of histamine extracted from whole blood must, I think, be difficult

to interpret physiologically. The blood is a tissue, and histamine held inactive in its cells need have no different functional significance from that locked up in the cells of solid tissues. Code's (1937) work in my laboratory seemed, at the stage which it reached, to be pointing to the eosinophil cells as the source of most at least of the histamine extractable from normal blood; and, though it is also true that the abundant layer of platelets obtainable from citrated rabbit's blood seems to be the rich source in that species, I venture to suggest that a more critical haematology might throw light on the still rather curious anomaly that rabbit's whole blood yields so much more histamine than that of other common species. Another point which would, I suspect, repay further investigation is that of the possibility of the formation of histamine from proteins by hydrolysis, whether by enzymes or by heating with acids (cf. Abel and Kubota, 1919). I believe that it would be useful to have more definite evidence on the extent to which solutions containing "incoagulable" protein products can be heated with acid with a certainty that the histamine found in the product will be only that which was preformed in the original blood or other material.

4. Lastly, it seems to me that it might have an important bearing on our conception of the proper and safe use of the antihistamines if the evidence for the concern of histamine in the vasodilatation of normal functional activity were clearer and more consistent. I raised the question of this as a possibility in a lecture in 1919, pointing out how the relaxation of capillary tone by histamine would make it the ideal agent of a fine adjustment of the circulation to local metabolic needs if we had evidence that it existed in the tissue cells and that it was liberated by their normal activity. We have evidence of its presence now, but the evidence produced by Anrep and his colleagues for its liberation from active muscle still lacks confirmation. I need hardly point out that failure to detect an increase of it in the venous blood does not of necessity exclude the possibility of its local liberation and local action. It might, however, suggest the possibility that in relation to antihistamines it would behave more like "intrinsic" than "extrinsic" histamine. In any case, I suggest that further attempts to settle the matter, perhaps by experiments under conditions not so close to those of natural circulation, might provide useful information, and that clear evidence on this point might give valuable warning or reassurance concerning the use of the antihistamines in practice.

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CAFFEINE AND GASTRIC SECRETION

BY

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The effects of caffeine on gastric secretion have recently been investigated in animals and in man by Roth and Ivy (1944a, 1944b, 1944c) and by Merendino *et al.* (1945). It has been shown that, although there is a wide variation in sensitivity between species, caffeine stimulates gastric secretion in man, cat, guinea-pig, and dog. Man is relatively sensitive to this action of caffeine, while the dog is rather resistant. The effect is probably exerted directly on the parietal cells.

Roth and Ivy (1944a) showed that the intravenous injection of 65–125 mg. of caffeine into cats anaesthetized with chloroform provokes a secretion of acid gastric juice for about 45 minutes. Later they reported (Roth and Ivy, 1944c) that caffeine and histamine act synergistically in stimulating gastric secretion in the cat. The effect was considerable, and in one animal a previously ineffective dose of histamine stimulated secretion of highly acid juice after injection of caffeine. The doses of caffeine used were themselves large enough to cause a secretion of acid gastric juice, and it was desirable to determine whether the effect of histamine was potentiated by smaller doses of caffeine which did not stimulate gastric secretion. This was particularly necessary, since doses of 125 mg. of caffeine are bordering on the toxic for the cat, and attempts to repeat the experiments of Roth and Ivy often resulted in early death of the animal. At the same time theobromine and theophylline have been compared with caffeine in respect of this relation to histamine.

Methods

The cat, anaesthetized with sodium pentobarbitone intraperitoneally, was prepared for continuous drainage of gastric juice by Roth and Ivy's (1944a) modification of Lim's (1923) method. Ligatures were tied around the cardia and duodenum and a cannula was inserted into the stomach through the pylorus (see Wood, 1948). Juice was collected in graduated centrifuge tubes, and the free and total acid was estimated by titration with N/50 sodium hydroxide, using thymol blue as indicator for both endpoints.

One hour after the completion of the preparation, secretion being basal (less than 0.05 ml. in 10 minutes), histamine acid phosphate was injected subcutaneously in a dose equivalent to 0.27–0.65 mg. of histamine (about 0.18 mg. per kg. of body weight). The resultant secretion of juice was measured at intervals of 10 minutes until the basal level of secretion returned.

The particular xanthine compound was then slowly injected intravenously over a period of two to five minutes. Solutions (1 or 2%) of caffeine sodium benzoate, theobromine sodium salicylate, and theophylline sodium acetate were used containing respectively about 1/2, 1/2, and 5/9 of caffeine, theobromine, and theophylline (w/w). Doses of caffeine were 10–20 mg. per kg. (20–75 mg. total dose), of theobromine 20 mg. per kg. (34–54 mg.), and of theophylline 20 mg. per kg. (42–62 mg.).

Two groups of experiments were done with caffeine. In one group of seven cats the second dose of histamine, the same as the first in any one cat, was injected 40–60 minutes after caffeine. This interval allowed enough time for any possible stimulant action of caffeine to pass off. Caffeine itself caused a significant increase in secretion in only three

of the seven cats. In another six animals the second dose of histamine was injected immediately after the caffeine. Collection of juice was continued until the basal level of secretion returned. The second dose of histamine was injected 40–60 minutes after theobromine or theophylline in all experiments with these substances.

Results

Caffeine.—Following the intravenous injection of 20 mg. of caffeine per kg. there was at first irregularity and some slowing of the heart and a transient fall of blood pressure. A temporary respiratory stimulation also occurred. Neither of these effects was so obvious after theophylline or theobromine; the blood pressure often rose about 10–15 mm. Hg after theobromine. Both the magnitude and duration of the histamine stimulation of gastric secretion were increased after caffeine (Table I). This was observed in all 13 experiments. In three of the seven cats where there was an interval of 40–60 minutes between the injections of caffeine and of histamine there was a mild stimulation of secretion due to the caffeine alone. Thus caffeine has a potentiating action which is still present 40–60 minutes after it has been injected. Since these doses of caffeine have only a slight, if any, secretory stimulant action, the two sets of results have been combined to obtain average figures from 13 animals. A typical graph of the secretory response to histamine before and after caffeine is shown in the Chart.

Theobromine and Theophylline.—Results with these two xanthine derivatives were much more variable than those with caffeine. The histamine effect was appreciably increased after theobromine in three out of six cats (Table II). In one of these (No. 90) free acid secretion due to histamine was increased from 1.2 to 36.25 ml. of N/50 HCl. In cat No. 93 theobromine had some stimulant effect itself, but there was no significant increase in the effect of histamine after theobromine. The smaller effect of histamine after theobromine in cat No. 89 cannot be attributed to the theobromine, since second doses of histamine often have less effect than the first dose. There was some

TABLE I.—*Secretion of gastric juice and free acid (in ml. N/50 HCl) due to histamine before and after intravenous injection of caffeine (10–20 mg./kg.)*

Cat No.	Secretion Due to								
	Histamine			Caffeine			Histamine after Caffeine		
	Juice (ml.)	Free Acid (ml.)	Duration (min.)	Juice (ml.)	Free Acid (ml.)	Duration (min.)	Juice (ml.)	Free Acid (ml.)	Duration (min.)
70*	0·35	0·0	40	—	—	—	4·0	15·7	60
71	2·65	4·75	70	—	—	—	2·95	11·05	90
72	0·95	0·6	40	—	—	—	2·05	7·15	70
73	1·6	1·8	80	—	—	—	5·85	23·0	80
74	1·55	3·6	60	—	—	—	4·15	15·0	60
75	1·5	0·0	60	—	—	—	4·85	5·6	110
76†	2·5	12·3	60	0·3	0·8	60	4·6	22·65	100
77	1·5	1·4	60	1·05	3·15	60	4·8	20·45	90
78	2·75	6·15	60	2·35	6·05	60	13·35	64·8	140
80	1·7	0·85	60	0·1	0·4	30	6·0	25·25	110
81	1·55	2·45	70	0·25	0·45	40	6·4	18·7	90
82	3·0	9·9	80	0·4	1·6	40	7·65	38·75	140
83	1·35	1·5	70	1·15	1·35	50	6·75	27·95	80
Average	1·8	3·5	62	0·8	2·0	49	5·7	22·8	94

* In cats Nos. 70–75 the second histamine dose was given subcutaneously immediately after caffeine.
† In cats Nos. 76–83 the second histamine dose was given subcutaneously 40–60 minutes after caffeine.

TABLE II.—*Secretion of juice and free acid (ml. N/50 HCl) in response to subcutaneous histamine before and after 20 mg. of theobromine per kg. intravenously.*

Cat No.	Secretion Due to								
	Histamine before Theobromine			Theobromine			Histamine after Theobromine		
	Juice (ml.)	Free Acid (ml.)	Duration (min.)	Juice (ml.)	Free Acid (ml.)	Duration (min.)	Juice (ml.)	Free Acid (ml.)	Duration (min.)
89	9·2	45·8	110	0·4	2·3	50	6·95	28·15	110
90	1·25	1·2	70	0·75	2·75	60	27·65	36·25	110
91	3·0	11·7	80	1·35	2·55	50	3·4	12·05	90
92	1·0	0·7	60	0·9	2·1	50	1·2	2·8	50
93	1·55	0·9	70	1·8	4·2	60	0·75	1·15	60
94	0·65	0·1	60	0·15	0	20	3·5	4·9	80
Average	2·8	10·1	75	0·9	2·3	48	7·2	14·2	83

TABLE III.—*Secretion of gastric juice and free acid (ml. N/50 HCl) in response to subcutaneous histamine before and after 20 mg. of theophylline per kg. intravenously.*

Cat No.	Secretion Due to								
	Histamine before Theophylline			Theophylline			Histamine after Theophylline		
	Juice (ml.)	Free Acid (ml.)	Duration (min.)	Juice (ml.)	Free Acid (ml.)	Duration (min.)	Juice (ml.)	Free Acid (ml.)	Duration (min.)
85	1·0	0·85	60	1·0	1·0	60	1·1	2·2	70
86	2·6	2·55	80	1·7	3·15	60	12·05	53·9	150
87*	2·15	4·65	100	0·3	0·7	50	0·15	0·25	40*
88	0·95	0·6	50	1·6	5·25	60	0·45	1·7	60
95	0·65	0·1	50	0·25	0·1	40	0·5	0·15	60
96	1·1	1·05	60	0·65	0·8	50	0·8	0	60
Average	1·4	1·6	67	0·9	1·8	53	2·5	9·7	73

* This cat died 40 minutes after theophylline.

secretory response after theophylline in two, or possibly three, out of six animals (Table III). In one of these (No. 86) the histamine effect was very greatly increased after theophylline, there being five-fold and twenty-fold increases respectively in the volume of juice and free acid secreted. In this animal theophylline itself had a stimulant effect on secretion. There was a possible potentiation in cat No. 85.

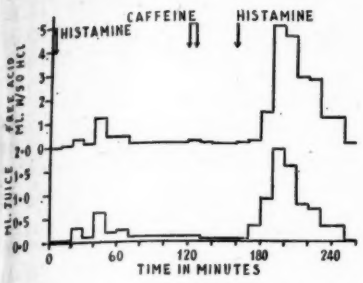

Chart showing the effect of histamine (0.35 mg. subcutaneously) on gastric secretion before and after a dose of caffeine (20 mg. per kg.) which did not stimulate secretion. Juice measured at intervals of 10 minutes (cat No. 81, weight 2 kg.).

The effect of histamine was less consistently altered after theobromine or theophylline than after caffeine, but occasionally there was a considerable increase.

Controls.—In control experiments repeated injections of a dose of histamine at intervals of one or two hours never gave an increasing response. Indeed, as Roth and Ivy (1944c) and others have indicated, there was a tendency towards a reduction in the secretory response to successive doses of histamine. Thus an increased effect of histamine after caffeine, etc., may be fairly attributed to the xanthine compound, but a reduction in the effect of histamine as in cats Nos. 87 and 89 is probably not due to the xanthine compound. Inspection of the gastric mucosa at the end of the experiment confirmed the findings of Roth and Ivy (1945). There was obvious hyperaemia and engorgement of the mucosa, particularly in those animals treated with caffeine. No quantitative estimate of the change was made, but it appeared much less after theophylline or theobromine. No similar effect was observed in the mucosa of any cat after repeated histamine injections or after continuous histamine infusion for several hours.

Discussion

Roth and Ivy showed that caffeine stimulates gastric secretion in the cat and also acts synergistically with histamine. They suggest that "the stimulation of gastric secretion may not necessarily be attributed to the same property of caffeine which is responsible for the synergism," since the synergistic action persists when the stimulant action of caffeine is over. The present results, showing that in doses which have no stimulant action on gastric secretion caffeine can potentiate the effect of histamine, support the probability that some other mechanism is responsible. Roth and Ivy (1945) have suggested that persistently increased blood flow accompanying vasodilatation might be a factor. Their later observations on the vascularity of the mucosa after caffeine strengthened this view. Observations on ulcers induced by caffeine in cats led them to suggest the following sequence of events caused by caffeine in the gastric mucosa: "vasodilatation and engorgement, vascular stasis, local anoxia, increased capillary permeability, transudation, exudation, and decreased cell nutrition." The vascular and cellular changes due to caffeine may make the mucosa more susceptible to the proteolytic action of acid and pepsin secretion.

The present results with theobromine and theophylline are less consistent and convincing. There is evidence that theophylline, at least, is a more potent vasodilator than caffeine, and it might have been expected to be at least as active as caffeine in potentiating the secretory action of histamine. To that extent this affords some evidence that the effect on blood flow is not necessarily the cause of the potentiating effect of caffeine. It is known that caffeine increases the oxygen uptake of resting frog muscle and that this increase is sensitive to azide (Stannard, 1939). It may be that caffeine also has some effect on an intracellular enzyme system concerned in gastric secretion, and this may underlie the potentiating effect of caffeine on histamine-induced gastric secretion. Whatever the explanation of the observed effect, certain conclusions are permissible. Even if histamine is not intimately concerned in either the physiology or pathology of gastric secretion, then consumption of large amounts of caffeine-containing drinks may be a factor in peptic ulcer formation or perpetuation. If histamine is associated with normal gastric secretion or with ulcer formation then the danger of excess caffeine intake is increased. It is still not justifiable, as Roth and Ivy (1946) stress, to conclude from the experimental results in animals that caffeine can cause peptic ulceration in man. It is known, however, that after a caffeine test-meal secretion of acid gastric juice is greater and more prolonged in ulcer patients than in normals (Roth, Ivy, and Atkinson, 1944).

The present experiments in normal cats show that caffeine potentiates the action of histamine on gastric secretion, and that theobromine and theophylline can have a similar action in some animals. Our results support Roth and Ivy's (1944b) conclusion that ulcer patients should restrict their intake of beverages containing caffeine, and also suggest that it is desirable to limit their consumption of foods and drinks containing theobromine and theophylline. These substances should equally be avoided by the patient with hyperchlorhydria but no ulcer.

Summary

Caffeine injected intravenously in a dose which does not usually stimulate gastric secretion in the anaesthetized cat consistently potentiates the gastric stimulant action of histamine.

A similar but less consistent effect was observed after theobromine and after theophylline.

The significance of these findings is discussed in relation to the management of the patient with peptic ulcer.

It is a pleasure to acknowledge the encouraging help given by Professor E. J. Wayne and the technical assistance of Mr. E. Salvin.

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Mr. John Edwards, Parliamentary Secretary to the Ministry of Health, paid tribute to the work of insurance committees when he addressed members of the London Insurance Committee on July 1 at their last meeting. "I think the finest tribute to their work is the decision to base much of the new health service on the existing arrangements. Without the co-operation of insurance committees it would have been very difficult for executive councils to prepare for the new scheme. They have most generously assisted executive councils from the very beginning by making the services of their staff available and by placing their offices and equipment at the councils' disposal. Wherever possible the Minister has included insurance committee members among his appointments to executive councils. I am quite sure that their experience will help to guide the councils over the difficult transitional period and ensure the continuity of administration which we are anxious to maintain." London, he said, had faced a special task: "Not only have you the largest register in the country but you also have the largest number of doctors and chemists in contract with you. I understand that there are 1,675 doctors on your list and that the chemists in contract with you have some 1,200 shops. Indeed, the magnitude of everything in London is always a challenge to those responsible for administration—a challenge which your committee has always successfully accepted."

RECTAL CANCER AND PRESERVATION OF FUNCTION*

BY

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No single standard operation is suitable for all cases of rectal or recto-sigmoid cancer, for the operation should be planned to suit the rectum rather than the rectum cut to suit the plan. The ideal is the efficient removal of the growth with preservation of normal defaecation. A permanent colostomy is not too high a price to pay for the efficient removal of a rectal cancer provided it is essential; it is a heavy burden if it is not. Clinical surgery suggests, and pathology supports the view, that in a number of these cases the internal sphincter, that mechanism of continent defaecation, is needlessly sacrificed through devotion to a stereotyped operation. At the same time it is salutary to remember that some surgeons have in the past abandoned anastomotic operations through the fear and the experience that such methods sometimes lead to an inefficient extirpation of the growth.

History

An operation to excise a rectal growth and preserve a functioning anus is no novelty; it is probable that it was a more fashionable ambition for the surgeon in the past century than it is now. Even a brief study of the literature on this subject makes it apparent that it would now be almost impossible to devise a truly original operation of this type, save perhaps in its minor details. The ingenuity of many surgeons has explored every conceivable route. Extensive reviews of the literature have been made by Bacon (1945), d'Allaines (1946), and many others. It will suffice here to mention some of the methods which seem to have influenced the present trend of surgical opinion.

It was not until the latter part of the last century that excision of the rectum became common. Though not the first, one of the more interesting of the early attempts to perform a resection-anastomosis on a rectal growth is that described by Maunsell in 1892. The rectum was mobilized through the abdomen and was then prolapsed through a dilated anal orifice to an assistant working in the perineum, who divided the outer layer of the prolapse, pulled down the growth, and performed a resection-anastomosis. Maunsell's immediate post-operative treatment consisted in making his patients drink large quantities of hot water, for he had found that he "had more success with hot water than with any other remedy." However unusual the post-operative treatment of half a century ago may seem to-day, the steps which Maunsell described have been the basis for many subsequent methods. Rayner (1935) quotes Sebrecht as utilizing the abdominal mobilization followed by the dissection upwards of the rectal mucosa from the mucocutaneous junction and the suture of the sigmoid to the anal canal. In 1908 Miles introduced the abdomino-perineal operation, and this discouraged attempts to restore anal function, at least in this country. In 1932 Babcock described the operation of procto-sigmoidectomy without preliminary colostomy, the salient features being the abdominal mobilization, excision of the lymphatic field at a high level, the perineal approach from within the external sphincter, and the removal of the internal sphincter, the sigmoid being brought out as a terminal colostomy through the anus. Devine (1937) advocated a preliminary transverse colostomy followed by resection and anastomosis on a clean and empty bowel. Dixon (1944) and Wangensteen (1945) have adopted a purely abdominal approach in suitable cases. Lockhart Mummery (1908), Pannett (1935), and others have described combinations of the abdominal and perineal approach, and Lloyd-Davies (1939) has described a "pull-through" method with drainage of the pre-sacral space through the anastomotic line.

It will be apparent from even this superficial survey that the surgeon who essays resection and anastomosis for a rectal growth has a wide choice of operation. Fortunately it is no shame to follow another's path: to be original it is necessary only to think for oneself and not necessarily unlike everyone else. He who constantly performs the same operation sometimes acquires not only dexterity in his particular method but a reluctance to attempt another. Certain aspects of this type of operation require special consideration; from these we must draw our personal conclusions.

The Sphincter Mechanism

Milligan and Morgan (1934) have made a careful study of the internal and external sphincters, and it is generally accepted that perfect continence requires an intact ano-rectal ring—that condensation of the circular muscle fibres of the rectum in association with the pubo-rectalis fibres of the levator ani muscle. It is true that Bacon and Babcock rely on the external sphincter for control after procto-sigmoidectomy, sutured round the sigmoid colon two to four weeks after resection. They state that 80% of their patients may be classified as continent, though 40% wear a protective perineal pad. While there can be no doubt that a varying degree of control may be obtained from the external sphincter even after it has been divided and repaired, certain continence requires an intact ano-rectal ring and, since the sense of perception is important, an intact lining to the anal canal. A good abdominal colostomy is probably better than an incontinent or untrustworthy anus.

Essential Pathological Requirements

We owe to Miles the first sound description of the pathology of rectal cancer and its implications on its surgical removal. He stressed the lymphatic spread upwards in association with the superior haemorrhoidal artery, laterally with the middle haemorrhoidal vessels, and downwards with the inferior haemorrhoidal vessels. Subsequent pathological studies, while bearing out the importance of the upward spread, have shown that Miles laid undue stress on the frequency of lateral and downward lymphatic spread. The work of Gabriel, Dukes, and Bussey (1935), Gilchrist and David (1938), and Coller, Kay, and McIntyre (1940) has shown that the main lymphatic spread of rectal cancer is in an upward direction, lateral and downward spread taking place only when the lymphatic system above is blocked by growth. Few lymphatic glands over 1 in. (2.5 cm.) below a rectal growth are likely to contain metastases, still less those 2 in. (5 cm.) below, and it would seem to be a reasonable conjecture that a distance of 2½ to 3 in. (6.25 to 7.5 cm.) below a growth is outside its lymphatic spread except in advanced cases. Here the involvement of the glands above the growth is likely to be such that complete removal of infected glands is impossible and any retrograde spread will be of secondary importance.

Dukes (1944) has demonstrated that 17% of rectal growths excised show involvement of the adjacent veins, though this does not necessarily denote hepatic metastases. He has also shown that the cancer cells may grow down the lumen of a vein in a retrograde manner, appearing sometimes as

*Based on a lecture delivered at the British Postgraduate School, Hammersmith.

a nodule of carcinoma in the mucosa below a growth. While this retrograde venous spread is probably uncommon, and such cases must inevitably have a rather poor prognosis, it is an additional reason for removing a margin of normal bowel below a growth.

There is a further pathological consideration to an operation of anastomosis. It is well known that adenomata are often found in the neighbourhood of a rectal cancer, and two primary growths are not uncommon. Some years ago, when pointing out the advantages of a purely abdominal resection for recto-sigmoid and high rectal growths in infirm patients, I drew attention to the possibility of another growth developing in the rectal stump (Muir, 1939). Gabriel and others have since recorded cases in which a carcinoma developed in this site after an abdominal excision. An abdomino-perineal or other combined operation removes completely the rectum and the greater part of the sigmoid colon, but the surgeon who performs an anastomotic operation must bear in mind the possibility, however small, of another primary growth developing from an adenoma in the rectal stump, or indeed in the remaining portion of the sigmoid colon. It is probable that the majority of patients would prefer to accept this risk rather than a permanent colostomy, but the presence of numerous adenomata below a high rectal growth should be regarded as a contraindication to the retention of any rectal mucosa and therefore to an anastomotic operation. The removal of all rectal mucosa, while it has other disadvantages, is in this respect a point in favour of the Babcock–Bacon operation.

The essential pathological requirements for an anastomotic operation are that the lymphatic drainage system of the rectum must be removed at its highest practical level by ligation of the inferior mesenteric artery either between the sigmoid branches or immediately below the last sigmoid branch; that the division of the bowel must be at least 2½ to 3 in. below the growth; and that the presence of numerous adenomata below the growth contraindicates this type of operation.

There are perhaps two occasional exceptions to these rules: the operable growth with small hepatic metastases, and the small growth in the rectal ampulla which clinically appears to be an "A" case. In both these cases there are strong grounds for trying to preserve a functioning anus even if such methods of resection necessitate a reduction in the margin of normal bowel below the growth.

Frequency of Cases Suitable for Resection-anastomosis

Bacon, analysing the site of the growth in 1,401 cases of rectal, recto-sigmoid, and sigmoid carcinomata, considered that over 80% were suitable for resection with preservation of a functioning anus. It should be remembered when considering these figures that Bacon accepts every growth 3 cm. above the ano-rectal line or 6 cm. above the anal margin as suitable for procto-sigmoidectomy, that the internal sphincter is not preserved in this operation, and that sigmoid growths are included in this series. Such sigmoid growths might well be those requiring ligation of the interior mesenteric artery for their proper removal, but even if they (315) are excluded, 1,086 cases of rectal and recto-sigmoid cancer remain. Of these, 231 were recto-sigmoid, 148 5 in. (12.5 cm.) and 211 4 in. (10 cm.) from the ano-rectal line. Thus 590, or more than half, might appear suitable, at least in theory, for a method of resection-anastomosis which preserved the internal sphincter.

Clinically, growths just palpable at the tip of the finger or discovered only on sigmoidoscopy are usually suitable. The prolapse of a recto-sigmoid growth may be misleading. A growth 2 to 3 in. above the cervix or vesicles may appear suitable, but in many cases a final decision can be made only at laparotomy. The rectum is not a straight tube, but undulates from side to side, lying curved in the hollow of the sacrum; a growth easily accessible on rectal examination may lie at the level of the abdominal wall when the rectum has been fully mobilized. In general, apart from being operable, growths suitable for these operations should lie at least 2 to 3 in. (5–7.5 cm.) above the lowest level of peritoneal reflection in the pouch of Douglas, though this peritoneal level is by no means constant in its distance from the ano-rectal ring. Growths of the rectal ampulla are unsuitable for operations of this type.

The Sigmoid Colon

Since it is necessary to ligate the inferior mesenteric artery either above or immediately below the last sigmoid branch, the blood supply to the distal sigmoid may be jeopardized. In one of my cases, intended for an anastomostic operation, ligation obliterated the arterial supply to the greater part of the sigmoid, and it became necessary to perform an abdomino-perineal resection. A good blood supply is essential to that part of the sigmoid which is to be brought down to the rectal stump or anal canal. After ligation some surgeons have advised marking the most distal part of the sigmoid with visible pulsation by means of a silk stitch. Poor vascularity is associated with infection and is far less likely to cause trouble when no actual suturing is used, as in "procto-sigmoidectomy," or when the operation is performed on a clean, empty, and non-functioning bowel.

A long and mobile sigmoid is of great assistance: an unusually short bowel or diverticulitis may render the operation impossible. The length of the sigmoid is of more importance in a "pull-through" method than in a purely abdominal resection and anastomosis, when sufficient bowel can usually be obtained by mobilizing it in the left iliac fossa. A pre-operative estimate of the length and condition of the sigmoid can be obtained by a barium enema.

Preliminary Colostomy

A preliminary transverse colostomy, as advocated by Devine, permits the operation to be performed on a non-functioning and, through the use of lavage and sulphaphthaladine, an almost sterile bowel. A left iliac colostomy "takes in slack" and reduces the mobility of the sigmoid.

A preliminary colostomy is not a routine in all methods. It is unnecessary in the Babcock–Bacon technique, where a terminal colostomy is established through the anus without bowel-suturing. Nor is it used by Wangensteen in his method of abdominal resection and anastomosis, employing deep pelvic clamps. d'Allaines performs colostomy at the time of the resection, on the grounds that a defunctionalized bowel is shorter, shrunken, and more difficult to anastomose.

Necrosis and infection are not only more likely but are also more dangerous when they occur in functional bowel. A preliminary colostomy will require closure, and its use may add three to four weeks to a patient's stay in hospital, but it adds such a degree of safety to these operations that I regard it as essential.

The Route

The necessity for removing the lymphatic field at its highest level makes abdominal mobilization an essential part of the operation. The resection may be carried out from the abdomen alone, thus requiring an anastomosis

between the sigmoid and the rectal stump in the depths of the pelvis, or the abdominal mobilization may be combined with a perineal anastomosis. This may be performed above the levator muscles, aided by their partial division, or outside the anal canal, by prolapsing the rectum, the growth, and the sigmoid through a dilated anus. Finally, as in procto-sigmoidectomy, the sigmoid may be brought out as a terminal colostomy through the anal orifice. My personal choice is for two methods: abdominal resection and anastomosis without clamps, which I believe to be applicable to the majority of suitable cases, and a "pull-through" resection, which, at least in my hands, requires a long sigmoid.

Abdominal Resection and Anastomosis without Clamps.—The use of clamps deep in the pelvis presents considerable difficulties. I have not had the opportunity of using those devised by Wangensteen for this purpose, but any clamp in this situation takes up valuable room and leaves devitalized tissues. I think it is therefore preferable to dispense with clamps for the purpose of the anastomosis. This operation is suitable for recto-sigmoid growths and many of those in the upper third of the rectum. A preliminary transverse colostomy is performed 14 days before the resection (combined with laparotomy if there is any doubt whether the case is suitable) and the distal bowel cleared by wash-outs and sulphaphthaladine emulsion. The first step in the resection consists in placing the patient in the lithotomy position and carefully swabbing out the rectum. The coccyx is removed and a corrugated drain introduced through the presacral fascia into the presacral space behind the rectum. Drainage should be provided for an anastomosis performed under some difficulty and surrounded by loose cellular tissue, and this is best obtained through the space left after excision of the coccyx. The patient is then placed in the full Trendelenburg position and the initial stages of the usual abdomino-perineal operation are performed. Before ligating the vascular pedicle the blood supply of the sigmoid loop should be carefully examined, bearing in mind the length of the mesosigmoid and the distance to which it must reach. As a rule I have ligated between the sigmoid branches where there is a long and mobile sigmoid and below the last sigmoid branch where the bowel is short.

The effect of this ligation will become evident on the sigmoid colon while the rectum is mobilized. This is carried out to a low level, anteriorly from the vagina or prostate, posteriorly, and laterally. A hysterectomy clamp, which takes up less room in the pelvis than any other, is applied 3 in. below the growth, and an assistant working from the perineum once more carefully swabs out that part of the rectum below the clamp. With the bowel on traction, the anterior wall of the rectum is now opened below the clamp (Fig. 1). Two cobbling "stay" sutures are inserted on each side (Fig. 2), the posterior wall of the rectum is divided, and two further sutures are inserted. These sutures serve to hold the rectal stump, to narrow the lumen of the rectal ampulla, which is larger than the sigmoid, and to prevent eversion. A point on the sigmoid with a good blood supply is selected, the mesosigmoid divided, and the sigmoid cut obliquely and anastomosed to the rectal stump (Fig. 3). Penicillin-sulphathiazole powder is sprayed around the anastomosis and the pelvis peritoneum is sutured over it and to the sigmoid colon.

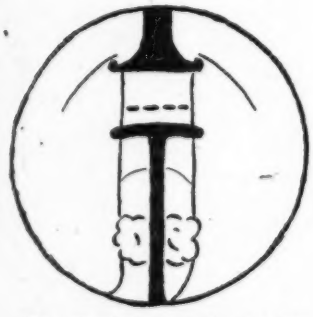

FIG. 1.—Clamp and retractor applied. The proposed line of incision in anterior rectal wall is shown.

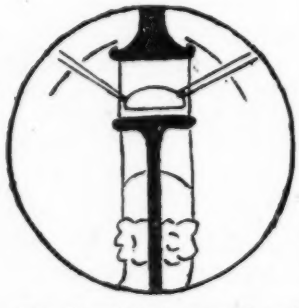

FIG. 2.—Anterior rectal wall divided. Two cobbling "stay" sutures are inserted.

The "Pull-through" Resection.—The essential features of this operation have been described. Its disadvantage is that a long sigmoid is of considerably more importance than in the preceding operation: its advantage, that it enables the surgeon to divide the bowel still closer to the ano-rectal ring. As an alternative to the "synchronous combined" position adopted by Lloyd-Davis (1945), the abdominal part may be first completed, the patient being subsequently placed in the lithotomy position. As in the preceding operation, I prefer drainage through the coccygeal space with complete suture of the anastomosis. After both these operations the transverse colostomy will require closure. Two to four weeks appears to be a suitable interval if the anastomosis is sound. I do not believe a long delay to be either necessary or desirable in the majority of cases.

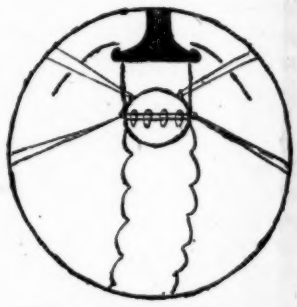

FIG. 3.—Four "stay" sutures are in position. Anastomosis with sigmoid has begun.

Results

The personal series here reviewed is of 86 consecutive cases of rectal and recto-sigmoid cancer operated upon since the war. Too small in number and too recent for any consideration of the end-results, they serve to show the frequency with which suitable cases may occur.

Abdomino-perineal or other combined operation	49
Abdominal resection and anastomosis	18
"Pull-through" resection and anastomosis	3
Abdominal resection (Hartmann)	1
Perineal resection (palliative)	1
Inoperable	14

Operability rate .. 84%

(Two patients upon whom resection was performed had small hepatic secondaries)

It will be seen that about one-third of the cases considered operable were found suitable for an anastomotic operation. I believe this percentage is too high: two of my cases should have had a combined operation. The abdomino-perineal is likely to remain the most common surgical attack against rectal cancer.

Complications.—Pelvic infection, fistula, stricture, and incontinence are the more serious complications which might follow these anastomotic operations. Necrosis of the rectal stump through interference with its blood supply has been described by Dixon. If the lateral ligaments of the rectum are fully divided the middle haemorrhoidal arteries must be severed and the rectal stump will depend mainly on the inferior haemorrhoidal arteries for its blood supply. These complications are less likely to occur and will be much less serious in their effects when the operation is performed on a non-functioning and "sterile" bowel. The last two patients upon whom I performed "resection-anastomosis" both developed fistulae. One of these was into the vagina, now happily healed, while the other was into the presacral space. These have been the only fistulae in this series.

The healed anastomotic ring, easily palpable on rectal examination, is always smaller than the rectal ampulla, since it is the junction with the sigmoid. I have had several cases with a small anastomosis, but none have yet required dilatation with bougies. All anastomotic cases have been left with full control. There has been some rectal prolapse after the operation in two of my cases, and this complication has been noted by others.

Mortality.—There have been two deaths in this short series, in which 72 cases were submitted to some form of resection. Assuming a high operability rate, all operations for rectal cancer must carry a definite mortality, having regard to the age group of these patients. However, the mortality has altered very considerably during the past 20 years. Those who had the privilege of watching Miles perform his operation know that this is not due to any improvement in surgical technique but to the surgical aids and in particular to the sulphonamides and penicillin. The danger from sepsis, considerable in the past, is now small. The mortality rate of these operations should now be not more than 5%.

End-results.—The end-results of operations for rectal cancer which preserve a functioning anus have been discussed by Babcock, Bacon, Dixon, and others. d'Allaines, after an exhaustive review of the published figures, concluded that the end-results were quite as favourable as those obtained by operations requiring a permanent colostomy. At the American Proctologic Society Meeting of 1947 Wangensteen (1948) described his results over a five-year period. He concluded that operations preserving the sphincter gave results equal to those obtained by the abdomino-perineal operation when the growth lay between 14 and 20 cm. from the anus, that the local recurrence rate in the surrounding pelvic tissues was too high to justify such operations for growths within 8 cm. from the anus, and that between 8 and 14 cm. the operation should be reserved for selected cases. Lloyd-Davies (1948) has recently described recurrences in "A" cases taking place at the suture line.

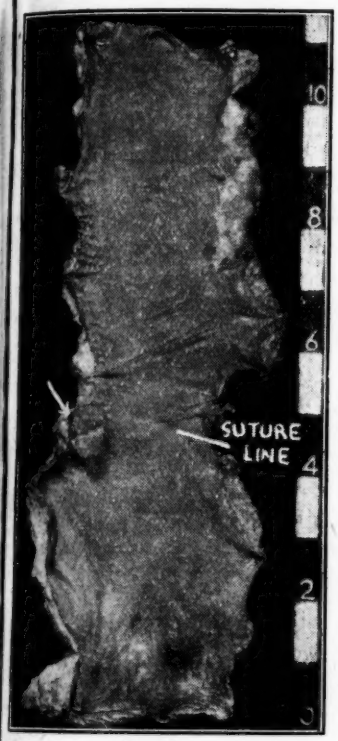

FIG. 4

I have at present a patient upon whom I performed an abdominal resection and anastomosis for a high rectal growth two years ago. Examination of the operation specimen showed that an adequate length of bowel had been resected; all glands examined below the growth appeared free, but metastases were present in a gland at the highest level. This patient, a woman of 59, recently developed a polypoid carcinoma at the anastomotic site and a full abdomino-perineal resection has now been performed (Fig. 4). I am indebted to Dr. Cuthbert Dukes for the following report.

The specimen measured 11 in. (28 cm.) and consisted of a portion of the pelvic colon and the rectum. The line of anastomosis from the original operation could be clearly seen about 3½ in. (8.75 cm.) above the ano-rectal line. There was a slight narrowing of the lumen in this region, but otherwise the mucosal surface looked normal except for a protuberant tumour half an inch (1.25 cm.) in diameter situated on the posterior quadrant. The tumour was attached to the mucous membrane by a broad pedicle, and from its general appearance it certainly seemed to be derived from the mucous membrane. In its gross characters the tumour appeared to be a pedunculated adenoma of doubtful malignancy. There was no evidence of extension into the adjacent perirectal tissues, which, however, were tough and fibrous.

Section shows the tumour to be an adenocarcinoma very well differentiated in character and, judged from its histology, of a relatively low grade of malignancy. There is evidence of spread to the submucous coat and slight invasion of the rectal muscle only. Sections cut through the thickened extra-rectal tissues show fibrosis and inflammatory infiltration but no sign of carcinoma. There was no sign of venous spread. Seven lymphatic glands were found and sectioned, but these were all free from metastases.

This is undoubtedly either a fresh primary tumour or the result of an implantation at the site of anastomosis of the previous operation.

If implantation is the cause of this type of recurrence it behoves the surgeon to exercise the greatest care in his technique, but it is a risk to which all bowel surgery for cancer must be exposed to some degree. By comparison I have two other patients who underwent an abdomino-perineal resection for rectal cancer within the past year and who have now developed fresh growths at and just above the terminal colostomy. These are surely examples of the inevitable and deadly trend of unhealthy and precancerous bowel. An abdomino-perineal operation will give increased protection against a further growth, but may not prevent it. Apart from the presence of obvious adenomata, our present knowledge does not allow us to predict when the retention of any rectal mucosa is fraught with any danger to a patient, though there are some who would say, "Always!"

Apart from the foregoing, it is germane to remind ourselves of several other points in the prognosis of rectal cancer. A high operability rate will almost certainly mean a reduced survival rate. It is known that if the lymphatic glands are not involved at the time of operation the prognosis is relatively good; in such cases the amount of bowel removed below the growth is not likely to affect the issue materially from this aspect. If at operation the glands are already involved the ultimate prognosis is less satisfactory, though considerably better with high removal of the lyphatic field than with a perineal resection. The operations which aim at the preservation of normal defaecation do remove the main lymphatic drainage system of the rectum to the same high level as an abdomino-perineal excision. If therefore a *judicious* selection of cases is made there is little reason why the results should not be comparable and a permanent colostomy be avoided in certain cases of rectal and recto-sigmoid cancer.

Conclusions

There is a sound pathological basis for operations which aim at preserving a functioning anus in high rectal and recto-sigmoid growths, but even in early cases and with adequate excision carcinoma can reappear at the anastomotic site.

To be certain of continence the ano-rectal ring must be preserved.

Of the various methods abdominal resection-anastomosis and a "pull-through" resection appear preferable.

A preliminary transverse colostomy lessens the risk and dangers of infection and should always be employed.

The use of sulphonamides and penicillin has reduced the mortality of all methods of rectal resection to a low figure.

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THE CLINICAL FEATURES OF MUSTARD-GAS POISONING IN MAN

BY

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The occurrence of general systemic symptoms following exposure to heavy dosages of mustard vapour or to massive liquid contamination was well recognized in the 1914–18 war. Since then experimental work on the subject has been largely concerned with the pathological changes observed in animals following the administration of mustard gas by different routes. These investigations have been reviewed by Smith (1943), who gives a comprehensive account of the literature.

In the absence of any large body of human experimental material, investigations on the changes in the haemopoietic system and blood chemistry of animals have tended to relegate to the background the clinical symptomatology produced in man by exposure to mustard gas. Isolated cases of accidental exposure have occurred from time to time, and some have been reported in the medical press (Hobbs, 1944). In these also, however, attention has been focused on the pathology rather than on the symptoms, many of which are nevertheless of the greatest importance, since their occurrence in the case of mustard-gas burns throws light on the mechanism by which similar symptoms arise following thermal burns.

It is difficult to demonstrate the occurrence of systemic manifestations in cases of slight or moderate mustard burns in temperate climates. In the Tropics, however, systemic poisoning by mustard gas is much more readily produced. From 1943 to 1945 I had the opportunity of observing a series of 438 volunteers exposed to mustard gas under tropical conditions, and thus of becoming familiar with the clinical picture of systemic mustard-gas poisoning.

Material and Methods

Of the 438 men observed 320 were exposed to mustard vapour and 118 to contamination by liquid mustard. In both the vapour and liquid groups the resultant burns were of all degrees of severity, ranging from a faint erythema of a localized area of skin to multiple ulcers many hundreds of square centimetres in area. All the men exposed to vapour and 77% of those exposed to liquid wore fully effective respirators throughout exposure.

The occurrence of systemic poisoning in these men was assessed both objectively, by daily clinical examination for a minimum period of 21 days after exposure, and subjectively, by daily interrogation. Each man was examined separately, and was asked only, "How are you feeling to-day in yourself?" No leading questions or suggestions were used.

Not all the symptoms of which the volunteers complained were easy to evaluate. Great care, however, was taken in each case to exclude adventitious causes, such as indulgence in the local mixture of lower alcohols, and to sort out genuine complaints from those which might be regarded as suspicious. In general, it was impossible to assign any accurate degree of severity to the subjective clinical symptoms owing to the variation in the general character and education of the volunteers. It is felt that considerable confidence can be placed in the findings, since they were recorded in men classified as A1 who were in good physical condition and well acclimatized to the Tropics. Further, the men had all volunteered to be exposed to mustard gas, and showed the keenest interest in the work.

Owing to lack of time and facilities it was only possible to follow blood changes in selected groups of men. The clinical pathology of some of the severely affected men was more extensively investigated.

Observations

Threshold and Severity

No symptoms attributable to systemic poisoning occurred in any vapour case in which no lesion more severe than erythema developed. There were 84 such men. Similarly, no man with liquid burns in whom the total raw surface ultimately produced was less than 20 square centimetres in area complained of systemic symptoms. In this category 83 men were included. Of the remaining 271 men, 102 reported one or more symptoms.

The severity of the effects varied within wide limits. In 35 men systemic manifestations were present on one day only, and in most of these cases the symptoms were in no way incapacitating. At the other extreme were cases in which systemic symptoms were a major factor in producing prolonged disability. In 37 men never more than one symptom was present, while the remaining 65 complained of two or more symptoms at various times. In general, the latter group included the more severely affected men.

Time Factors

Of the 102 men affected 66 (65%) showed symptoms within 24 hours of exposure; 83 (81%) were involved within 48 hours and 96 (94%) before the sixth day. It is also of interest that only 3 (16%) of the 19 cases in which the onset of symptoms occurred later than 48 hours after exposure could be described as more than very slightly affected. In contrast the onset of systemic symptoms in some of the worst cases preceded even the appearance of erythema of the skin.

Fig. 1 shows the number of men complaining of one or more systemic symptoms on each day after exposure. The number is largest on the first day, and falls fairly regularly till the end of the second week. No complaints were received from any man after the forty-fifth day. It is interesting that there is no correlation between the number of men complaining of systemic symptoms and the severity of the skin burns. Characteristically, the latter developed slowly, and in the vapour cases did not reach their maximal development until, on the average, 11 days after exposure. This time appeared to be independent of the severity of the lesions (Sinclair, unpublished work,

1944). The time taken by the liquid burns to attain their maximum varied considerably, but in general was somewhat shorter. Considering the group as a whole, there was a steady rise in the extent and severity of the skin lesions

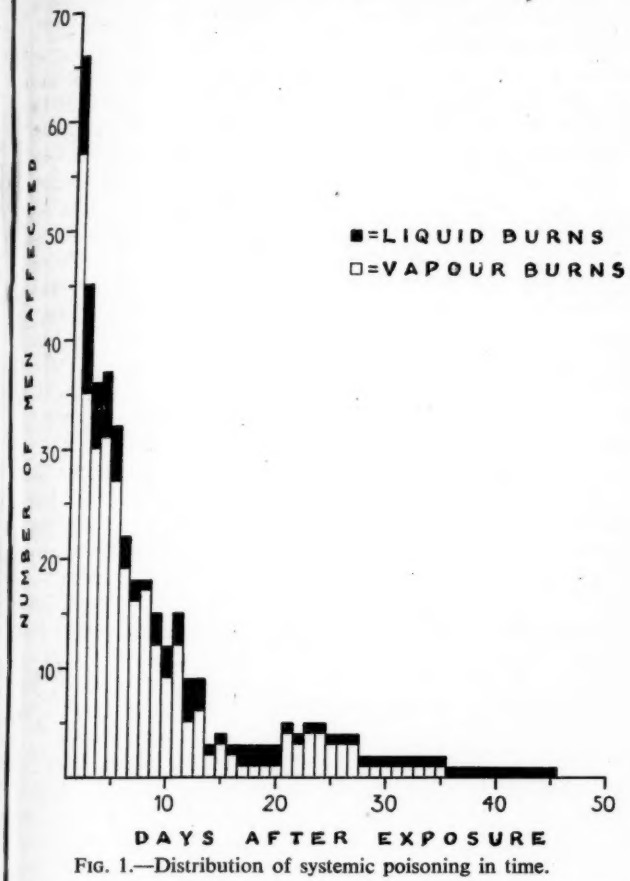

FIG. 1.—Distribution of systemic poisoning in time.

until the eleventh day, whereas during this time there was a steady fall in the number of systemic symptoms recorded.

Symptoms and Signs

Table I sets out the various symptoms observed in this series. It is evident that most of them might be produced by any state of general intoxication, and are not in any way peculiar to mustard-gas poisoning. Two rather more unusual signs—tremor and tachypnoea—were restricted to severely burned cases. Table I also shows, for each symptom, the percentage of the total number exhibiting systemic symptoms who complained of that symptom. It will be seen that there is a striking agreement in these percentage figures between the vapour and the liquid cases, thereby indicating that the overall clinical picture of each group of men was similar in spite of the differences in the type of skin lesion and its mode of production.

TABLE I.—*Relative Incidence of Symptoms*

Symptom	Vapour Cases		Liquid Cases		All Cases	
	No. of Men Complaining	Percentage Complaining (out of 86)	No. of Men Complaining	Percentage Complaining (out of 16)	No. of Men Complaining	Percentage Complaining (out of 102)
Nausea	50	58	11	69	61	60
Headache	36	42	6	38	42	41
Lassitude	33	38	6	38	39	38
Insomnia	26	30	5	31	31	30
Vomiting	16	19	3	19	19	19
Anorexia	14	16	5	31	19	19
Abdominal pain	13	15	1	6	14	14
Diarrhoea	9	10	2	13	11	11
Tremor	5	6	2	13	7	7
Vertigo	6	7	0	0	6	6
Tachypnoea	4	5	1	6	5	5
"Anxiety state"	1	1	2	13	3	3
Total no. complaining of one or more symptoms	86		16		102	

TABLE II.—*Distribution of Individual Symptoms in Time*

Period	No. of Complaints of											Total
	Nausea	Vomiting	Anorexia	Abdominal Pain	Headache	Lassitude	Insomnia	Tachypnoea	Diarrhoea	Vertigo	Tremor	
First day	41	10	3	3	18	12	4	5	1	4	6	107
Remainder of first week	82	7	17	18	37	47	53	—	11	1	9	282
Second week	15	7	17	14	12	11	24	—	3	1	7	111
Third week	2	—	14	2	3	1	—	—	—	—	7	29
Fourth week	5	—	12	15	6	—	—	—	1	—	7	46
Fifth week	—	—	7	7	—	—	—	—	—	—	7	21
Later than fifth week	—	—	—	—	—	—	—	—	—	—	10	10
Total	145	24	70	59	76	71	81	5	16	6	53	606

The clinical picture of systemic poisoning showed, nevertheless, a considerable variation with time. Table II shows the number of complaints made of each symptom during different periods after exposure. A consideration of this table shows, for example, that on the day after exposure nausea and vomiting between them accounted for 47.7% of the total number of complaints made on that day, whereas complaints of anorexia and abdominal pain taken together accounted for only 5.6% of this total. Thereafter, however, there is a gradual decrease in the proportion of complaints due to nausea and vomiting, while the proportion due to anorexia and abdominal pain steadily rises with time. Other symptoms show proportional changes which are less striking. Thus the percentage of total complaints due to headache remains fairly constant, and complaints of lassitude and insomnia are practically restricted to the first two weeks.

It may therefore be said that in the first week following exposure the most characteristic complaint was of nausea with or without vomiting, whereas after the beginning of the third week anorexia and abdominal pain accounted for the greater part of the complaints made.

To evaluate the relative frequency with which any given symptom "presented," a simple marking system was adopted. One mark was allotted to each man, and if there was only one presenting symptom the whole mark was entered under this symptom. If several symptoms presented simultaneously the mark was split proportionately between them. By this procedure it was found that nausea with or without vomiting was the commonest presenting symptom, receiving 38.3 marks. Headache and lassitude each received 22.8 marks, and all the other symptoms together accounted for the remaining 18.1 marks.

Individual Symptoms and Signs

Nausea and Vomiting.—Of all the symptoms which have been recorded in man after exposure to mustard gas nausea and vomiting are the commonest (Norris, 1918; Moorhead, 1919; Wilson and Mackintosh, 1920; Soltau and Elliott, 1923; Aitken, 1943; and others). Vomiting is also frequent in experimental animals (Lynch *et al.*, 1918; Warthin and Weller, 1918; Smith, 1943). It has already been noted that nausea was the commonest individual symptom of the present series. A characteristic feature of the nausea was the occurrence of intermissions. Thus one man was nauseated on the first day, and then had no symptoms of any kind until the sixth day, when he had an attack of

severe nausea lasting four days. The onset of this attack preceded by two days a generalized outbreak of vesication. The complaints of nausea recorded in Table II in the fourth week after exposure were received from a group of men exhibiting abdominal symptoms in whom nausea accompanied the other complaints.

Vomiting was always preceded and accompanied by nausea. In the worst case there was repeated vomiting and retching over a period of 48 hours. It will be noted that in Table II vomiting is recorded several times during the second week. The circumstances of such delayed vomiting were carefully examined, but it was necessarily difficult to exclude factors other than the effects of mustard. It is possible that in some instances the vomiting may have a partly functional origin (Wilson and Mackintosh, 1920; Soltau and Elliott, 1923).

Headache.—Headache of the type described by Moorhead (1919), Soltau and Elliott (1923), and Aitken (1943) was a feature of many cases. It was characteristically frontal, continuous rather than remittent, resistant to medication, and of a peculiarly unpleasant nature. In some of the worst cases headache was responsible for a considerable amount of disability. For example, one man complained of intense headache from the first to the third day, sufficient to make him cry out and to necessitate his admission to hospital on the fourth day. The headache disappeared on the seventh day, but from then until the fifteenth day intermittent nausea, vomiting, vertigo, insomnia, and anorexia were present. On the twenty-first day the headache reappeared in an even more severe form than before, and lasted until the twenty-seventh day. This man suffered from mustard burns which were only moderate in degree, but it was necessary to retain him in hospital solely because of his systemic manifestations. It is probable that he represents an unusual degree of sensitivity to mustard-gas poisoning.

Lassitude.—Lassitude has been noted as a feature of mustard cases by Moorhead (1919), Wilson and Mackintosh (1920), and Aitken (1943). In the severe cases in this series the men were most unwilling to do anything more in their spare time than lie down and try to sleep. This finding has the more weight since it was recorded on Australian fighting troops in the absence of pain or severe burns. It might be expected that the occurrence of lassitude would run parallel to that of insomnia, but in only 12 of the men were lassitude and insomnia both present, and in only 5 of these were the two symptoms recorded simultaneously. It is evident, therefore, that the lassitude could not be attributed solely to loss of sleep.

Insomnia.—Before attributing insomnia to the specific action of mustard gas it is necessary to exclude the factors of pain, irritation, or itching arising from the skin burns. It is probably for this reason that insomnia has rarely been mentioned as a symptom of mustard poisoning (von den Velden, 1921). Nevertheless, in their initial stages mustard burns are relatively painless (Soltau and Elliott, 1923). In 12 of the 16 more severely affected men the onset of insomnia occurred before the third day, and it is noteworthy that none of these men advanced the reason of discomfort as the cause of his complaint. It is possible, however, that insomnia occurring later was, at least in part, due to pain or irritation.

Anorexia and Abdominal Pain.—Reference to Table II shows that complaints of loss of appetite occurred not only in the first few days, as might perhaps be expected in any series of skin burns, but also as late as the fourth and fifth weeks after exposure. At the beginning of the fourth week a condition supervened in 4 men which was characterized by anorexia, abdominal pain, and occasional nausea. Abdominal pain was also recorded in the early stages (Table II), but was usually not so severe as in the delayed cases. In the literature epigastric pain appears frequently as an early and acute symptom of mustard-gas poisoning (Mandel and Gibson, 1917; Moorhead, 1919; Soltau and Elliott, 1923; Chiesman, 1944), but its occurrence in the later stages does not appear to have been mentioned. Hobbs (1944) has described ulceration of the duodenum in a fatal case of mustard-gas poisoning, and the nature of the delayed pain observed in this series is of interest in this connexion. It occurred from half an hour to an hour and a half after meals, and lasted for a few hours. It was usually a steady ache, situated in the epigastrium and accompanied by a diffuse epigastric tenderness. It was not relieved by food, but could be alleviated by alkali; it did not interfere with sleep. Flatulence and heartburn were not observed, and the pain bore no relation to the type of food consumed.

Diarrhoea.—Diarrhoea was in all cases mild and of short duration. Both Soltau and Elliott (1923) and Wilson and Mackintosh (1920) are emphatic that diarrhoea in gassed cases in the 1914–18 war was due to associated conditions rather than to mustard-gas poisoning. Moorhead (1919) mentions diarrhoea of a dysenteric type, but states that constipation was the rule. Nevertheless, diarrhoea is a prominent feature in experimental animals (Lynch *et al.*, 1918; Smith, 1943), and it has been regarded as a leading symptom of systemic intoxication by mustard gas (Smith, 1943). In this series detailed records were not kept of controls, but it may be said that diarrhoea was certainly not more common in the volunteers than in the camp staff, who were living and working under similar conditions.

Tremor.—The occurrence of tremor has been described in experimental animals following the intravenous injection of mustard gas (Warthin and Weller, 1918), but, except for one case mentioned by Wilson and Mackintosh (1920), does not appear to have been particularly noted in man. In this series it was restricted to severely burned men, in whom it appeared within a few hours of exposure. In all the vapour cases affected it involved the whole body, especially the hands, and at its worst resembled well-marked shivering. The men did not, however, complain of feeling cold, and the body temperature was in all cases normal. The tremor was coarse and showed frequent remissions; it was not under voluntary control. The deep reflexes were invariably exaggerated, but examination of the central nervous system disclosed no other abnormalities. In all cases the tremor disappeared within 48 hours. In one man with liquid burns an exactly similar tremor was noted on the second day after exposure. In another a coarse tremor of the hands and fingers was present throughout his stay in hospital (45 days). This man had severe multiple third-degree burns in 30 distinct areas. These areas were such as to preclude any testing of the usual deep reflexes in either legs or arms. He was, however, extremely unsteady and incoordinated. He became nervous and excitable, and his mental condition during the first few weeks approximated to an anxiety state. Examination of the central nervous system was negative, and by the time his burns had healed adequately the deep reflexes were normal.

Vertigo.—Vertigo has been noted by Aitken (1943) in vapour cases, and was present in six vapour cases in this series. It did not occur apart from nausea, and never lasted longer than one day.

Tachypnoea.—In four of the five vapour cases with tremor tachypnoea began within a few hours, at the same time as erythema appeared. Nine hours after exposure the resting recumbent respiratory rate had risen in all four to 30 per minute or over, and in one case to 40 per minute.

Breathing was in all cases shallow and fairly regular, and there was no evidence of dyspnoea. Twenty-four hours after exposure there was no disturbance of respiration in any man.

One of the men severely burned by liquid also complained of considerable "breathlessness" during the first 24 hours, even while lying in bed. It is interesting to note that an increased respiratory rate has been reported in goats following the contamination of the skin by 40–50 mg./kg. of liquid mustard (Allen, Cameron, Coles, and Rutland, unpublished work, 1944). These authors state that the respiratory rate "may reach high levels between the sixth and twelfth hours." Similar results were reported by Lynch *et al.* (1918) in dogs. It is therefore probable that the tachypnoea seen in human cases is due to a direct action of absorbed mustard derivatives rather than to any non-specific cause connected with skin damage. Both Mandel and Gibson (1917) and Norris (1918) mention rapid breathing as an early symptom in mustard-gas casualties, but in the men they describe it is apparent that protection of the respiratory tract was inadequate, and that the rapid breathing was the first sign of bronchitis. Moorhead (1919) and Aitken (1943) note the occurrence of pain in the chest, probably from the same cause.

Anxiety State.—Reference has already been made to the occurrence of a well-marked anxiety state in one of those severely burned by liquid mustard. Two other men, both badly burned, showed a very similar condition for the first two weeks after exposure. All three were "jumpy," irritable, and restless, and were afraid that they were going to die. In all cases recovery was rapid once the lesions had demonstrably started to heal. These men presented a marked contrast to the tired listlessness characteristic of many others in this series. Restlessness and irritability are described by von den Velden (1921), while Wilson and Mackintosh (1920) mention a case in which "mental excitement" was prominent.

Temperature : Pulse : Blood Pressure.—Cases of marked toxaemia were sometimes accompanied by an irregularly raised temperature, which did not exceed 101° F. (38.3° C.). This was not associated with sepsis, which was very uncommon in this series. The pulse rate in such men was correspondingly increased. Elevation of the pulse rate on the first day usually appeared to be due to the effort of retching.

In Moorhead's series (1919) the blood pressure was often low, while in Aitken's cases it was slightly raised. In four cases of liquid poisoning in this series there were signs of surgical shock, accompanied by evidence of haemoconcentration and a rise in the blood non-protein nitrogen, but in none of these could the blood pressure be satisfactorily taken owing to the position of the burns on the arms and thighs.

Clinical Pathology

One of the most characteristic effects of severe intoxication by mustard gas is a gradual fall in the number of circulating leucocytes, with concomitant changes in the bone marrow (Needham, Cohen, and Barrett, 1947). In fatal cases a condition amounting to aleukaemia may precede death (Hobbs, 1944). In none of the men in this series was there any definite evidence of a leucopenia, but in some of the severely burned cases there was a statistically significant temporary fall in the ratio of neutrophil polymorphs to lymphocytes. A polymorphonuclear leucocytosis, attributable to the presence of raw skin surfaces, occurred in many cases of vapour poisoning about the end of the first week and lasted for about ten days.

Moorhead (1919) observed that in mustard-gas poisoning the coagulation time of the blood was often markedly decreased. This observation was confirmed in a number of vapour and liquid cases in this series. Fig. 2 shows the course of the mean coagulation time for a group of ten men exposed to mustard vapour. It was unfortunately not possible to investigate the cause of this rapid coagulation of the blood.

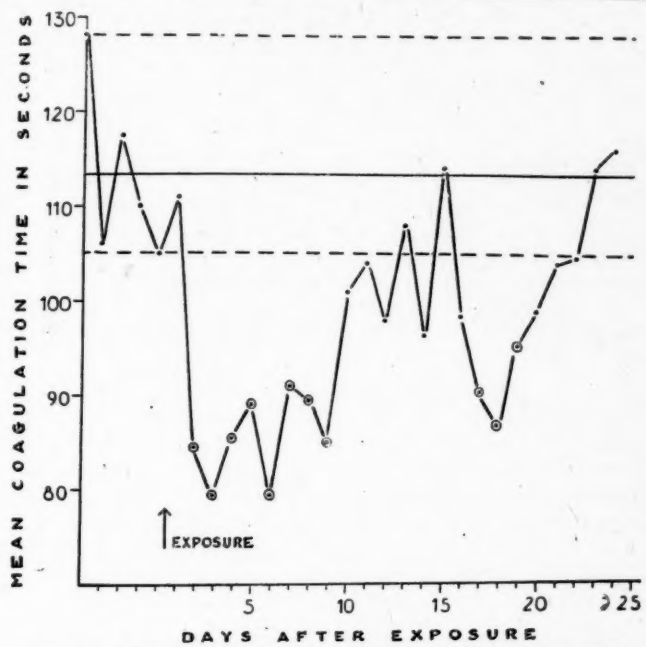

FIG. 2.—Effect on blood-coagulation time. The course of the mean blood-coagulation time in 10 men exposed to mustard vapour. The day of exposure is indicated by an arrow, the limits of the pre-exposure values by interrupted lines, and the mean pre-exposure value by a continuous line. Points on the graph showing statistically significant departures from this mean are circled.

In view of the occurrence of "abdominal" symptoms, and of the known association of peptic ulcers with mustard-gas burns (Hobbs, 1944), an investigation of the total and free acidity of the gastric contents was carried out by Thompson (unpublished work, 1945) on a number of men in this series. He concluded that "under the conditions prevailing . . . exposure to mustard gas gives rise, in a proportion of cases, to a significant increase in the secretion of acid by the gastric mucosa." The rise in acidity was not immediate, and the maximum figures tended to occur about the eleventh day. No investigations on the gastric acidity of the men complaining of abdominal symptoms in the fourth week were carried out.

Even in the most severely burned men in this series no abnormal changes could be demonstrated in the sedimentation rate, the platelet count, or the composition of the urine.

Discussion

Lynch *et al.* (1918) were among the first to suggest that many of the symptoms observed in men gassed by mustard were due to the action of mustard gas as a specific systemic poison. At the time it was believed by many that the effects were caused solely by the local tissue damage. Thus Soltau and Elliott (1923) state that "vomiting . . . is due to the swallowing of saliva or nasal secretion which has been infected by mustard gas"—an explanation which was also accepted by Aitken (1943). Warthin and Weller in 1918 found "no evidence of any systemic poisoning by the absorption of dichlorethyl sulphide from the skin, eyes, or mucous membranes of the respiratory or gastro-intestinal tracts." Subsequent work, however, has left no doubt that mustard gas has a specific toxicity, manifested particularly by its effect on the haemopoietic tissues, irrespective of the route by which it is administered (Smith, 1943).

In 1943 work on the exposure of human volunteers in Australia showed that severe systemic symptoms could be produced despite the fact that fully effective respirators were worn throughout exposure. This condition also applies to all the cases reported in this paper, with the exception of five of the men exposed to liquid contamination, who wore eye-shields instead of respirators. The only possible channel of entry for mustard derivatives into the body was thus the intact skin. It follows that the symptoms and pathological changes observed can only be due either to the action of derivatives of mustard circulating in the blood after having been absorbed through the skin or to the absorption of non-specific metabolites from the damaged skin.

The latter explanation cannot be wholly neglected. Gibson and Brown (1944), reporting on shock following thermal burns, state that vomiting was frequent and often severe. Further, many of the symptoms occurring in the cases exposed to mustard are, by reason of their general character, difficult to attribute solely to the action of mustard derivatives. Nevertheless it is probable that the observed picture is for the most part due to this cause, for several reasons:

1. It has been shown that the systemic symptoms in experimental animals exposed to mustard vapour or to liquid skin contamination can be almost exactly reproduced by the intravenous injection of pure mustard or derivatives of mustard (Smith, 1943).

2. In this series the symptomatology of vapour and liquid cases was exactly similar in spite of the marked differences in the type of skin burn produced.

3. In the present series 65% of the men affected became so within 24 hours, and in very few of these was the degree of skin damage greater than an erythema by the end of this time. Indeed, in some cases the onset of nausea preceded the appearance of erythema. It is thus difficult to explain the symptoms solely on the basis of the liberation of toxic metabolites by skin damage. Further, in the group as a whole the severity of the skin lesions showed a progressive increase until the eleventh day, whereas during this time the number of systemic symptoms steadily fell.

4. The leucopenia characteristic of severe poisoning by mustard gas, however administered, is not produced by other, non-specific, substances injurious to tissues.

It is reasonable, therefore, to regard most of the findings in these men as being due to the specific action of mustard. There is one group of symptoms, however, which may be in part due to a non-specific mechanism. Peptic ulcer is a well-recognized complication of thermal burns (Harkins, 1938), and it seems possible that the association of abdominal pain, anorexia, and nausea which occurred in a few of the men during the fourth week after exposure was in some way related to the skin damage rather than to mustard poisoning. The number of cases examined by Thompson (1945) is too small to show any definite relation between symptoms referable to the gastro-intestinal tract and the appearance of hyperacidity, but the findings merit further investigation.

The mechanism by which the mustard derivatives which have been found in the blood stream of experimental animals act to produce clinical manifestations is obscure, except that there is a specific toxic effect on the bone marrow (Needham, Cohen, and Barrett, 1947). It is possible that many of the apparently diverse symptoms produced in man have a common pathological origin. It must be pointed out that the results in this series show that systemic intoxication in both liquid and vapour cases occurs much more readily in the Tropics, probably owing to a generally enhanced power of the skin to absorb mustard gas (Cullumbine, 1948).

Not all the symptoms and signs observed had the same practical importance with reference to disability. In this respect the incapacitating potentialities of nausea, vomiting, and headache may be emphasized. The necessarily limited clinical pathological investigations in this series showed that, although changes in the leucocyte count and in the blood coagulation time were noted, these changes were in no instance such as to cause concern, and did not affect the clinical course of the cases.

Summary

An account is given of the various clinical symptoms and signs encountered in 102 cases of mustard-gas poisoning observed in the Tropics.

These symptoms followed the absorption of mustard gas through the skin, and were in great part the result of a specific toxic action of mustard derivatives.

Severe systemic manifestations were produced in some instances, although the blood changes found were in all cases clinically unimportant.

The incidence of systemic symptoms was greatest on the day after exposure, and fell progressively thereafter.

The commonest individual symptom was nausea, in the more severe cases accompanied by vomiting. The possible relation of abdominal symptoms to a disturbance of gastric secretion is discussed.

Potentially incapacitating symptoms occur in the Tropics very much more readily than in temperate climates.

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The Board of Trade reports that the President of Finland has submitted a Bill to the Diet proposing the establishment of a Government Company for the importation and distribution of medicinal preparations on a wholesale basis. The share capital of the company is to be 100 million Finmarks, but can be raised to 300 million Finmarks. The Government will hold all shares with the exception of two, which could tentatively be transferred to the Public Pension Board and the Helsinki University. In the preamble to the Bill the Government states that as long as the importation and distribution of medicinal preparations are solely in the hands of profit-seeking private companies there is always the danger that prices will be too high. It is therefore essential that the trade should also be conducted by a company whose objects are entirely confined to promoting the public welfare. As the Government company will sell the products at the lowest possible prices it will force the competing firms to make corresponding reductions in prices. The new company will also handle the distribution of medicinal products to the State and municipal hospitals.

TREATMENT OF TYPHOID CARRIERS WITH PENICILLIN AND SULPHATHIAZOLE*

BY

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Chemotherapy has hitherto yielded very disappointing results in the treatment of typhoid carriers, and radical surgical treatment is by no means regularly effective. Bigger (1944, 1946) described a synergistic action of penicillin and sulphathiazole against various organisms, including *Salmonella typhi*; and Comerford, Richmond, and Kay (1946, 1947) treated two carriers with a combination of these drugs with apparent success. It was decided to treat a larger series of known chronic typhoid carriers with the same two drugs to see if the beneficial results could be regularly expected.

Experiments were carried out at the same time to determine the sensitivity of strains of *Salm. typhi* to penicillin and sulphathiazole and to decide if penicillin is excreted in the bile in concentrations sufficient to influence the growth of *Salm. typhi*.

Sensitivity of Strains of Salm. typhi to Penicillin and Sulphathiazole in vitro

The sensitivity of the strains of *Salm. typhi* from the carriers to the separate and combined actions of penicillin and sulphathiazole was tested in nutrient broth treated according to the method described by Harper and Cawston (1945). One batch of culture medium was used throughout. Sixteen strains were tested—five of Vi-phage Type A, five of Type C, four of Type E1, and two of Type N (Craigie and Felix, 1947). Recently isolated cultures were maintained on Dorset's egg medium, and inocula for the *in-vitro* tests were prepared by two successive subcultures in broth at four-hourly intervals. Inocula varying from 5,000 to 1,000,000 organisms were subjected to the action of different concentrations of the drugs in 5 ml. of broth. The absence of turbidity after incubation for 48 hours was recorded as evidence of inhibition. A quantitative estimate of the bactericidal effect of the drugs was then made by subculturing various quantities from the original tubes into fresh medium containing an excess of penicillinase and para-aminobenzoic acid.

The results of the *in-vitro* tests may be summarized as follows.

1. Penicillin alone in a concentration of 8 units per ml. inhibited the growth for 48 hours of 11 out of 16 strains. The remaining 5 were inhibited by 16 units per ml. Complete sterilization was achieved by slightly higher concentrations, 12 strains being sterilized in 48 hours by a concentration of 16 units per ml. and 4 strains by 32 units per ml. These results were more or less independent of the size of the inoculum between 5,000 and 1,000,000 organisms and of the Vi-phage type.

2. The action of sulphathiazole alone was dependent upon the size of the inoculum. With small inocula of 5,000 to 10,000 organisms 7 strains were sterilized in 48 hours by a concentration of 1.25 mg. of sulphathiazole per 100 ml., 4 strains required a concentration of 2.5 mg. per 100 ml., and 5 strains 5 mg. per 100 ml. An inoculum of 100,000 organisms was regularly inhibited by a concentration of 5 mg. per 100 ml., but a lethal action in 48 hours was not common. With inocula of 1,000,000 organisms a concentration of 5 mg. per 100 ml. rarely inhibited growth.

3. When the joint action of the two drugs was examined the concentration of sulphathiazole was kept constant at 5 mg. per 100 ml., the concentration of penicillin and the size of the inoculum being varied. As small inocula (5,000 to 10,000 organisms) were sterilized in 48 hours by a concentration of 5 mg. of sulphathiazole per 100 ml. no studies were made of any possible joint action of the two drugs. With large inocula (1,000,000 organisms) the presence of penicillin in small amounts together with 5 mg. of sulphathiazole per 100 ml. often inhibited growth, but a sterilizing action was seldom demonstrable. Complete sterilization of the inoculum in most cases was achieved only when the concentration of penicillin approximated to that which would bring about this effect unaided by sulphathiazole. As an approximate measure it could be stated that the presence of sulphathiazole in a concentration of 5 mg. per 100 ml. reduced to one-half the concentration of penicillin required to effect sterilization of an inoculum of 1,000,000 organisms.

Penicillin in Bile

Evidence was sought that penicillin is excreted in bile in sufficient concentration to kill *Salm. typhi* or at least to inhibit its growth. A tube was passed into the duodenum of a healthy subject who was receiving intramuscular injections of 500,000 units of penicillin every three hours. Ten minutes after the fourth injection a sample of bile aspirated after the administration of magnesium sulphate as a cholagogue contained more than 100 units of penicillin per ml. and the Oxford staphylococcus was inhibited by a 1 in 6,000 dilution of the bile in broth. The bilirubin content of this sample was 150 mg. per 100 ml. A similar examination in another person yielded a sample of bile containing more than 20 units of penicillin per ml.

A number of examinations were made of samples of bile from patients whose gall-bladders had been removed by surgical operation. In one patient a fine catheter was led into the cystic duct and left there for several days for the collection of samples of bile. After the second intramuscular injection of 500,000 units of penicillin the bile contained 25 units per ml., inhibiting the growth of the Oxford staphylococcus at a dilution of 1 in 1,280, and a concentration of 12 to 25 units was steadily maintained thereafter. A similar result was obtained in a patient whose gall-bladder was drained to relieve an empyema. Initially, this patient was given intramuscular injections of 100,000 units every three hours, and after 12 hours the fluid from the gall-bladder inhibited the growth of the Oxford staphylococcus at a dilution of 1 in 64 (approximately 1 unit), but *Salm. typhi* was not inhibited. The dose of penicillin was increased to 500,000 units every three hours, and 12 hours afterwards the concentration of penicillin in the bile was between 10 and 20 units per ml. The bile inhibited the Oxford staphylococcus at a dilution of 1 in 1,000 and *Salm. typhi* at a dilution of 1 in 8. In a third patient the contents of the gall-bladder excised one hour after a single intramuscular injection of 1,000,000 units of penicillin contained 12 units per ml.

There was thus evidence that penicillin is excreted in the bile in adequate concentrations to inhibit or destroy *Salm. typhi* if injections of the order of 500,000 units are given at intervals of three hours.

Therapeutic Trial

Seventeen faecal carriers of *Salm. typhi* were selected for treatment. There were five carriers of Vi-phage Type A, five of Type C, four of Type E1, and three of Type N.

*Based on a report to the Medical Research Council.

All were known to be regular excreters of *Salm. typhi*, as specimens of faeces had been examined in our laboratories at monthly or in some cases weekly intervals for very long periods. A single batch of yellow penicillin (Glaxo) was used for the majority of the cases, but in two who were given injections of 5 million units it was necessary to use crystalline penicillin.

Three different courses of treatment were tried; the results of these are shown in detail in the accompanying table.

Courses of Treatment for Typhoid Carriers

Course	Case No.	Known Duration of Carrier State	Vi-phage Type	Total Dosage		Result	
				Pen. (mill. units)	Sulph. (g.)		
1	1	6 years	A	30	45	Positive	11th day
	2	6 ,,	C	30	45	,,	9th ,,
	3	6 ,,	E1	28	25	,,	30th ,,
	4*	6 ,,	E1	30	45	,,	14th ,,
	5	15 ,,	E1	30	40	,,	8th ,,
	6	5 ,,	C	30	45	,,	7th ,,
	7	4 ,,	C	30	45	,,	7th ,,
	8	5 ,,	E1	30	45	,,	7th ,,
2	9	6 ,,	C	48	72	,,	6th ,,
	10	6 ,,	C	48	72	,,	1st ,,
	11	3 ,,	A	60	70	,,	119th ,,
	12	14 ,,	A	60	70	,,	1st ,,
	13	4 ,,	A	60	70	,,	1st ,,
	14	9 ,,	N	60	90	,,	28th ,,
	15	7 ,,	N	60	90	Negative	48 weeks
	16	6 ,,	N	60	90	Positive	12th day
	4*	6 ,,	E1	60	90	Negative	36 weeks
	5	15 ,,	E1	65	86	Positive	6th day
	6	5 ,,	C	60	90	,,	7th ,,
	14	9 ,,	N	60	90	Negative	36 weeks
3	13	4 ,,	A	120	36	Positive	1st day
	17	4 ,,	A	120	36	,,	1st ,,

* Cholecystectomy two years before treatment.

Course 1. Continuous 5-Day Course.—In the continuous course of treatment 1,000,000 units of penicillin were injected intramuscularly and 1.5 g. of sulphathiazole were given orally every four hours for five days. The total course thus consisted of 30 million units of penicillin and 45 g. of sulphathiazole. Seven patients were so treated. An eighth patient received 28 million units of penicillin in doses of 500,000 units every three hours for seven days and a total of 25 g. of sulphathiazole. Seven of the eight cases were found to be excreting typhoid bacilli within two weeks of the end of treatment. The remaining case was found positive on the 30th day, but as the patient had left hospital a few days after the end of treatment no specimens were received between the 7th and 30th days.

Course 2. Intermittent 21-Day Course.—The intermittent course of treatment was designed at the suggestion of Professor J. W. Bigger. It consisted of the same four-hourly doses of penicillin and sulphathiazole in four courses each lasting two and a half days, the individual courses being separated by intervals of two to four days. The total dosage as planned was thus 60 million units of penicillin and 90 g. of sulphathiazole, but in some instances slight adjustments were necessary. The precise amounts given to the patients are shown in the table.

Eight patients received the intermittent course in the first instance. Four of these gave positive cultures within one week of the cessation of treatment, one became positive on the 28th day, and one on the 119th day. One case due to Vi-phage Type N has remained negative for 48 weeks to date and represents the only apparent success in the first 16 cases treated by a single continuous or intermittent course.

After a short interval four patients were selected for a further trial by the full intermittent course. Three of them had previously had the continuous course and one the intermittent course. Two of these four patients were positive again within a week of the termination of the second course. The other two were still negative 36 weeks after the treatment. It will be seen that two of the successes were obtained in Vi-phage Type N carriers, but a third carrier of this type (almost certainly the same strain) was not cured (Case 16). Two of the cured carriers who had harboured Vi-phage Type N showed a definite drop in their typhoid Vi-agglutinin titre. The Vi-agglutinin titre of the third apparently cured carrier (Vi-phage Type E1) has so far remained unchanged.

Course 3. Intermittent Course with Massive Doses of Penicillin.—When the results of the above attempts were reviewed it was decided that there was little ground for optimism, and no conclusion could be reached regarding a dosage which might be expected to give encouraging results. In a final attempt two carriers were treated with injections of 5 million units of penicillin together with 1.5 g. of sulphathiazole orally every three hours for 24 hours, the total daily dosage being 40 million units of penicillin and 12 g. of sulphathiazole. The patients were so treated on three occasions, separated by rest intervals of three days. Each carrier therefore received a total of 120 million units of penicillin and 36 g. of sulphathiazole. One of these cases had been previously treated by the ordinary intermittent course of 21 days (Case 13 of the series), but the other had not previously been treated by penicillin or sulphathiazole. Both patients remained positive, and excretion of typhoid bacilli did not cease even temporarily.

In-vitro tests with the carrier strains isolated before and after treatment showed that they had not altered their resistance to penicillin and sulphathiazole.

Summary and Conclusions

Attempts were made to clear 17 chronic typhoid carriers of infection. At first eight cases were given a continuous course of treatment similar to that employed successfully by Comerford *et al.* (1946) in two cases. All eight cases resumed excreting typhoid bacilli soon after the end of the course of treatment.

When it became apparent that the continuous treatment was not as effective as had been hoped it was decided to try an intermittent course suggested by the work of Bigger (1944) as a method of eliminating "persisters." Accordingly much larger amounts of both drugs were given over a period of 21 days with rest intervals, and in eight cases there was one apparent success. Soon afterwards four of the unsuccessfully treated cases were selected for a further trial by this method, with two more apparent successes.

In order to decide if yet larger doses might succeed, two cases, one of which had been previously treated, were given 40 million units of penicillin and 12 g. of sulphathiazole a day on three occasions. Both attempts were unsuccessful.

Although the results of *in-vitro* tests suggested that typhoid carriers might be cleared of infection by some combination of penicillin and sulphathiazole the results of the therapeutic trial were not encouraging. There were only three apparent successes out of 17 cases in spite of the very large amounts of penicillin and sulphathiazole used.

We are indebted to the superintendents and medical staff of several hospitals and to several medical officers of health for their willing co-operation in making this trial. We are grateful to Dr. A. Felix, F.R.S., for much co-operation and helpful criticism of this work.

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Seven holders of United Nations Social Affairs Fellowships from Greece, India, the Philippines, and Poland arrived in London on July 19 to spend from three to six months in Britain on courses of study arranged by the British Council. Social Affairs Fellowships are awarded to those directly concerned in work of reconstruction and rehabilitation. Typical subjects of study are welfare in industry, child welfare, social aspects of tuberculosis, and juvenile delinquency. Lectures are being given on such subjects as health services, rehabilitation and resettlement of the disabled, the organization of welfare in industry, employment exchange services, the work of a borough council, the Education Act of 1944, housing management, town planning in London, administration of justice, delinquency and probation, and social security. Visits will be made to the Houses of Parliament; County Hall; St. Helier's Hospital, Carshalton; an employment exchange; the Minerva Housing Estate, Bethnal Green; and a meeting of Holborn Borough Council.

PARATYPHOID OSTEOMYELITIS

REPORT OF TWO CASES

BY

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Paratyphoid osteomyelitis is uncommon. We found only 21 cases recorded in the literature at our disposal. The following two case reports present some interesting features: the first patient was an infant, and in the second case there was an unusually long period between the initial infection and the appearance of the osteomyelitis.

Case 1

A female infant aged 1 year was seen at the out-patient department on Feb. 19, 1947. The mother reported that the child had been feverish for three weeks, although the temperature had not been taken. On examination a tender swelling of the left shoulder was found and a preliminary diagnosis of osteomyelitis was made. The following day the child was admitted to the paediatric department. The past history was not significant.

Examination showed a well-developed child in a fair state of nutrition, with a temperature of 37.5° C. (99.6° F.) on admission. The liver was felt three fingerbreadths and the spleen one and a half fingerbreadths below the costal margins. Over the left acromio-clavicular region a soft swelling the size of a walnut was noted. The skin over the swollen area showed increased venous markings and fluctuated on palpation. The temperature of the affected area did not seem higher than that of the surrounding skin. No other abnormal findings were discovered on physical examination. The blood count on Feb. 21 was: 3,400,000 erythrocytes, 19,400 leucocytes (neutrophils 34%, monocytes 2%, lymphocytes 58%, band forms 6%, no eosinophils). Routine urine examination was negative.

The diagnosis of osteomyelitis was confirmed by radiograph, and penicillin treatment was started (60,000 units daily). Aspiration of the swelling on Feb. 21 yielded 2 ml. of red-streaked pus, a direct smear of which showed Gram-negative rods. Culture of the pus on MacConkey's medium produced a fine growth of non-lactose-fermenting colonies of a motile Gram-negative bacillus. By the usual routine sugar reactions and an agglutination test the organism was identified as *Salm. paratyphi B* (Schottmüller). A second aspiration five days later again yielded a pure culture of *Salm. paratyphi B*. This was also isolated from the urine and faeces. On Feb. 25 a blood culture was negative and a Widal test showed paratyphic B 1 in 500. Agglutination of the serum with own strain was positive at 1 in 5,000.

Penicillin treatment had no apparent influence on the course of the disease, and in view of the bacteriological findings it was discontinued. The further clinical course was uneventful; the swelling gradually decreased and 12 days after admission the child was discharged from hospital, but remained under observation. In a few weeks she made a complete recovery, confirmed by radiographs and by function of the affected shoulder.

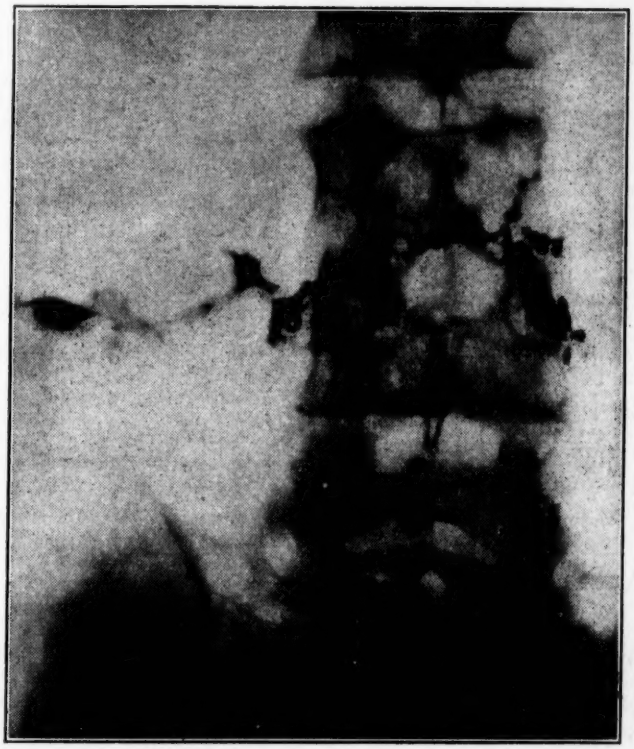
Case 2

The patient was a 48-year-old man born in Turkey. At the age of 15 he fell from a height and injured his loin. One year later he suffered from enteric fever, which lasted about 10 weeks. During convalescence from this disease he began to suffer from pains in his thighs and loins, which became so severe that he was unable to move. His physician told him that he was suffering from "coxalgia" and he was put in plaster for six months. After removal of the plaster he felt well and there was no restriction of movement in the affected joints. Since that time he had always been in good health, except for pneumonia 12 years ago, from which he recovered without any complications.

The patient was operated upon for bilateral inguinal hernia in August, 1946. A few weeks later he began to feel pains in his thighs and loins. At the same time his temperature became subfebrile (37.5–38.5° C.). The pain and fever lasted for three weeks, and he received penicillin treatment for 10 days in another hospital without result. On Oct. 18 he was admitted to the medical department of this hospital.

On examination he appeared pale and chronically ill. The only definite abnormal physical sign was a pronounced tenderness in the right loin and in the right hypogastric region. The temperature was 37.5° C., the pulse 100, the blood pressure 110/60 mm. Hg. There were no other abnormal physical signs. Laboratory examination showed: urine, no sugar or albumin; deposit, nothing of importance; blood: urea, 21 mg. per 100 ml.; sugar, 89 mg. per 100 ml.; Kahn test, negative; erythrocytes, 4,550,000; Hb 75% (Sahli); leucocytes 17,000 (neutrophils 71%, monocytes 3%, lymphocytes 23%, band forms 2%, eosinophils 1%); E.S.R. (Linzenmeier), 40 minutes; Weltman coagulation band, 3. Radiographs of the gastro-intestinal tract, chest, and urinary tract showed nothing abnormal. Blood culture and agglutination test for brucellosis were negative. Widal test showed 1 in 200 for *Salm. paratyphi B* only. A radiograph of the lumbar spine showed union of the bodies of the third and fourth lumbar vertebrae.

In view of the marked tenderness in the right loin, the persistent temperature (37.5–39° C.), the rapid sedimentation rate, and the shift of the Weltman band to the left the possibility of a perinephric abscess was considered. An exploration of the perirenal tissues was made by Dr. E. Joseph on Oct. 29, but no pus was found. After the operation the temperature



The intervertebral disk between the third and fourth lumbar vertebrae is almost destroyed. Synostosis between these two vertebrae. In the region of the intervertebral space a cavity is seen towards which a fistula leads from the right loin.

fell to normal and there was some improvement in the general condition, although the blood sedimentation rate remained high. A fortnight after the operation the patient was discharged.

The following day a sudden rise of temperature occurred and the pain in the right loin reappeared. Two days later he was readmitted to hospital. Examination then revealed a hot well-defined swelling below the scar of the recent operation. This swelling was tender to the slightest pressure. A superficial incision (Dr. E. Joseph) yielded a large amount of pus. On

microscopical examination Gram-negative rods were seen, and on culture the isolated organism proved to possess the biochemical and serological properties of *Salm. paratyphi B* (Schottmüller). The same organism was isolated from another specimen of pus taken a few days later. The patient's serum agglutinated the organism isolated from his pus at a titre as high as 1 in 5,000. Urine and faeces yielded no growth of *Salmonella*. After the operation the temperature dropped, the E.S.R. became less rapid, and the patient greatly improved. When he was discharged from hospital on Dec. 12 the incision wound had almost healed. He reported back to the out-patient department a few weeks later complaining of pain in the right loin and renewed fever in the evenings. Into a small opening which remained in the incision scar lipiodol was injected, and an *x*-ray film showed communication with a cavity which tomography revealed between the third and fourth lumbar vertebrae (see illustration). Since then the patient has been seen repeatedly. When the fistula stops discharging the pain and fever reappear, but cease when drainage is re-established.

Comment

According to various statistics, almost 1% of cases of typhoid are complicated by osteomyelitis: 0.82% according to Winslow (1923), 0.87% according to Keith and Keith (1926). The reported incidence of this complication in cases of paratyphoid is much lower. Webb-Johnson (1917) saw only two instances of bone involvement in 1,038 cases of paratyphoid. Winslow (1924) in 100 cases of paratyphoid observed no case of osteomyelitis. Ross Veal and McFetridge (1934) collected 16 cases from the literature and added two of their own. Their series does not include the cases of Reenstjerna (1910). Two additional cases have since been reported (Just, 1937; Jetter, 1938). Our two cases bring the total number recorded up to 23. From the historical point of view it is interesting to recall that *Salm. paratyphi B* was first isolated —even before its definite identification by Schottmüller— from an osteomyelitic lesion of the sternoclavicular region by Achard and Bensaude (1896).

Osteomyelitis, both typhoid and paratyphoid, is rare in children. Winslow (1923), who collected all bacteriologically proved cases, found only four cases between the ages of 2 and 10. A typhoid abscess of the spine in a 3-year-old child was reported by Abbassy (1946). We were unable to find in the literature an instance of typhoid or paratyphoid bone abscess in infants. Our case of paratyphoid osteomyelitis in a 1-year-old infant seems to be the youngest recorded.

In Case 2 the abscess presented itself clinically 32 years after an attack of enteric fever. The coxalgia for which the patient at that time was put in plaster was apparently a paratyphoid spondylitis. The localization in our patient was typical, as the lumbar spine is involved in about 70% of cases showing spine lesions (Ross Veal, 1939).

The affinity of the typhoid and paratyphoid bacilli for the bone marrow invites consideration. The bacillus is already found in the bone marrow at the beginning of the infection (Storti and Filippi (1937). There is also good clinical and experimental evidence to show that the bacillus may persist in the marrow for a very long time (Dmochowski and Janowski, 1895; Lüdke, 1909; Coplans, 1936; Ling *et al.*, 1940; MacDonald, 1941; Kernwein and Capps, 1943).

Ten cases of typhoid osteomyelitis have been reported in the literature in which the time interval between disease and the bone complication exceeded ten years. We found only one case of paratyphoid osteomyelitis reported in which the bone abscess appeared 20 years after the original disease (Jensen and Kock, 1913).

What are the factors involved in the sudden exacerbation of an infection after so long a latent period? Most authors agree that trauma may upset the equilibrium between the bacilli and the defence mechanism of the body. The traumatic agent need not be a direct blow. Undue strain or fatigue, pyrexia, or anything likely to lower the body's capacity for defence may cause the latent infection to flare up and show itself clinically. In our case the herniotomy may well have acted as such a trigger mechanism.

Summary

Two cases of paratyphoid osteomyelitis are reported, one occurring in a 1-year-old infant and the other in an adult 32 years after the initial infection.

Factors contributing to abscess formation and the incidence of this complication are discussed.

We are indebted to Dr. J. Gurevitch, head of the department of bacteriology and serology, and to Dr. A. Druckmann, head of the *x*-ray institute of our hospital, for their help.

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SALM. ORANIENBURG SEPTICAEMIA

REPORT OF A FURTHER CASE

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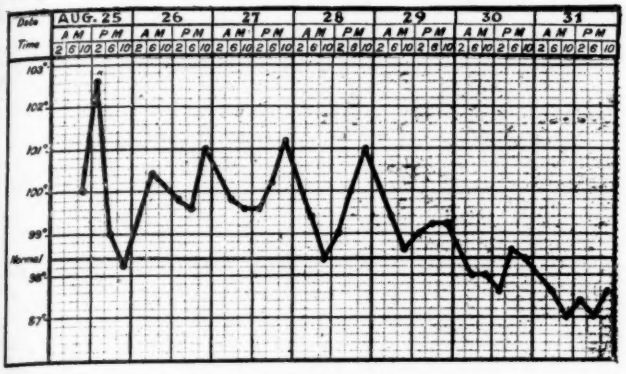
County Pathologist, Dorset

In the first recorded case of *Salmonella oranienburg* blood infection in Britain the source of the infection was never discovered (Kerrin, Elder, and Smith, 1935). In the light of events in the recent war, when *Salm. oranienburg* contamination of transatlantic dried egg was shown to be common, this original infection may well have been imported, for in 1935 food flowed in plenty to this country from all over the world.

A subsequent case was reported by one of us (Cooper, 1944), but, although intestinal infections with this Salmonella are not uncommon, blood infection has rarely come to light. For this reason we venture to publish a further case met with in this laboratory. There were strong reasons for suspecting dried-egg infection as the cause of the 1944 case, but at that time it was ruled impolitic to say so. In our present case no history of dried-egg consumption could be obtained, but presumably this substance is an ingredient of a variety of creams and sauces which may be consumed in hotels and restaurants. The old view that the carrier state was rare in salmonella infections is no longer tenable. Our present patient was shown to be a convalescent carrier for over five weeks. Food-borne infections of human origin are therefore probable.

Case History

The patient, an unmarried woman aged 21, was first seen by her doctor on Aug. 22, 1947, having returned on Aug. 19 from a holiday in Jersey, where she spent Aug. 16 in bed with headache, diarrhoea, and vomiting. The headache had persisted, and the doctor's view on the 22nd was that the patient was clinically likely to be suffering from typhoid fever. Next day he therefore requested the county laboratory to undertake a blood culture. At that time the patient's bowels were constipated. Pyrexia, lassitude, and headache persisted for a further nine days. There was no rash and the spleen was never palpable. The temperature chart is here shown; the pulse was



Temperature chart of case.

of the order of 70 to 80 throughout. The headache, associated as it was with stiffness of the neck muscles and the incidence of an outbreak of poliomyelitis at the time, brought in the exclusion of that condition as a further problem. There was no history of the patient having had dried egg in a form she was able to recognize, but she had partaken of salad dressings while on holiday.

We withdrew 20 ml. of blood : 5 ml. was put into 100 ml. of bile-salt broth, 5 ml. into 100 ml. of glucose-proteose peptone No. 3 which contained "liquoid" and para-aminobenzoic acid, 5 ml. into Wintrobe mixture, and 5 ml. of clotted blood was used for the Widal test. Growth appeared in the glucose-proteose after 48 hours' incubation. No growth appeared in the bile-salt broth. Subculture produced a non-lactose-fermenting Gram-negative bacillus which was motile and grew freely in taurocholate media.

Acid and gas developed in glucose, maltose, mannite, and dulcite—all within 24 hours. There was no reaction in lactose, saccharose, or salicin, but a slight acid reaction in litmus milk. The indole test was negative. Gelatin was not liquefied.

Agglutination reactions : polyvalent *Salmonella A*, negative ; polyvalent *Salmonella B*, negative ; polyvalent *Salmonella C*, positive titre 1 in 250 ; *paratyphosum C* "O," positive titre 1 in 50. An organism isolated from the stools on Aug. 23, 24, 30, and Sept. 5 and 29 produced identical results. The first negative result was obtained on Oct. 25, and all three subsequent stools were negative. The organisms recovered from the blood and faeces were confirmed by Dr. Joan Taylor as conforming to *Salm. oranienburg*.

A blood count on Aug. 23 showed : haemoglobin, 92% ; red cells, 4,630,000 ; leucocytes, 6,600 (polymorphs : neutrophils 70%, monocytes 4%, lymphocytes 26%). Urine taken on Aug. 23 was negative biochemically and bacteriologically. Widal reactions were negative.

Discussion

Kerrin *et al.* (1935) give a similar clinical story of their case, but hypostatic pneumonia and death occurred. Their blood culture was positive in taurocholate media. Cooper's (1944) patient presented as a case of gastro-enteritis with continuing pyrexia. This case also continued to excrete the organisms for at least 55 days. In our own case it is reasonable to suppose that infectivity of the faeces ceased midway between Sept. 29 and Oct. 25—about 40 to 50 days after the organism was first detected on Aug. 23.

Summary

A further example of the isolation of *Salm. oranienburg* from blood is recorded.

The value of blood culture in cases of pyrexia of unknown origin is re-emphasized.

The discovery by the same laboratory of two cases of blood infection with this organism draws attention to the occurrence of septicaemia in at least a proportion of salmonella infections.

REFERENCES

Cooper, T. V. (1944). *Mon. Bull. Min. Hlth.* **3**, 40.
Kerrin, J. C., Elder, A. T., and Smith, J. (1935). *Lancet*, **1**, 1042.

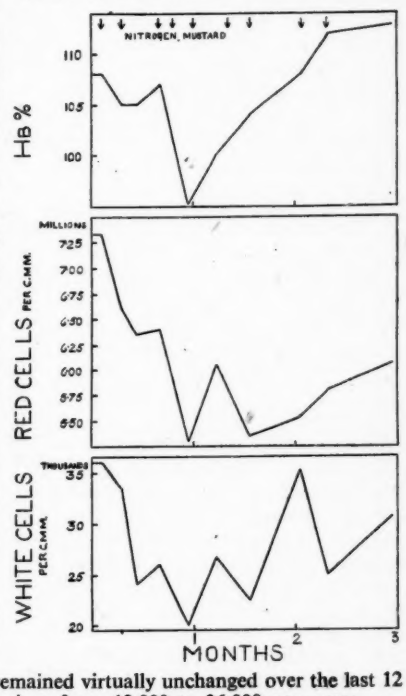
Medical Memoranda

Nitrogen Mustard in Polycythaemia Vera

Since Wilkinson and Fletcher (1947) reported the results of treatment of three cases of polycythaemia vera with nitrogen mustard the opportunity for treating a further case has occurred.

Case Report

The patient, a woman aged 51, had been a known sufferer from this condition since she had been admitted under the care of Professor Nattrass in 1935. At that time she complained of high facial colouring of four years' duration, with pain in the left side and nausea, dyspnoea, and palpitation of two years' duration. The haemoglobin was 106% (Haldane), the red blood cells numbered 7,910,000 per c.mm. and the white blood cells 12,000 per c.mm. The spleen was palpable 2 in. (5 cm.) below the left costal margin. No treatment was then given. In December, 1947, she again reported, stating that although the nausea had disappeared she had had increased pain in the left side of the abdomen for six years, and during the last year the palpitation and dyspnoea on exertion had been more marked. Infrequent fainting attacks had also occurred. No cardiovascular abnormality was detected and the blood pressure was 150/90. The spleen was now palpable 10 in. (25 cm.) below the left costal margin. The haematological state is shown in the accompanying charts. It is noteworthy that though the haemoglobin and red cells had remained virtually unchanged over the last 12 years the white cells had risen from 12,000 to 36,000 per c.mm.



The patient was given methyl-bis(β-chlorethyl)amine hydrochloride intravenously in doses of 0.1 mg. per kg. of body weight on the 3rd, 8th, 19th, 23rd, 28th, 37th, 43rd, 57th, and 64th days after coming under observation. Apart from nausea and vomiting, which came on three hours after each injection and lasted for two to three hours, no untoward side-effects of the treatment were encountered. As will be seen from the charts, the haemoglobin level and the red and the white blood cell counts dropped during the first month and thereafter there was a pronounced tendency for these values to increase in spite of treatment. There was no significant alteration in the size of the spleen during the three-months period of observation. The patient stated that she experienced slight alleviation of her symptoms during the first two months.

This case falls into line with two of the three cases of polycythaemia vera in Wilkinson's series in which the therapeutic response to nitrogen mustard was unsatisfactory.

I wish to thank Professor Nattrass, Royal Victoria Infirmary, Newcastle-upon-Tyne, for permission to publish this case, and Dr. W. A. R. Thomson, of Boots Pure Drug Co., Ltd., for the supplies of nitrogen mustard.

A. W. WOODRUFF, M.D., M.R.C.P., D.T.M.& H.

REFERENCE

Wilkinson, J. F., and Fletcher, F. (1947). *Lancet*, **2**, 540.

Reviews

VISIBLE SPEECH

Visible Speech. By Ralph K. Potter, George A. Kopp, and Harriet C. Green. (Pp. 441; illustrated. £1 5s.) New York: D. Van Nostrand Company, Inc. London: Macmillan and Co. 1947.

An important and indeed almost Utopian project has been launched successfully. The research workers at the Bell Telephone Laboratories show in this book how a machine can translate the sounds of speech into patterns which the eye can learn to interpret. A startling principle has been proved, and the imagination is roused by the possibilities which this opens up. The authors wisely do not exploit this emotional appeal; instead they describe in a careful and matter-of-fact way what has been achieved, how it was done, and how much more work will be required before the implications can be fully understood.

"Visible speech" as described in this book is a representation of sound according to frequency, intensity, and time. That such a representation could retain all the intelligence contained in the sound has long been appreciated; it is in fact similar to the analysis presumed to take place in the inner ear. But what is new is the experimental proof that the visual representation can be learnt and interpreted. Some experimenters have achieved considerable competence in this, and the authors give illustrations and a carefully devised commentary to enable the reader to learn the first steps for himself. The reader can thus obtain a clear idea of the processes of learning this new symbolism and assess the difficulties involved.

The authors discuss the possible application of this type of technique to problems of deafness, and these suggestions seem to promise much. Teaching the deaf has always been an arduous task, and this work may well become the foundation of an entirely new method. Though little work with the deaf is yet on record the authors mention the case of one congenitally deaf man who learnt by this technique to use a telephone. An extension of the technique may even result in the portable "translator" as a permanent aid for the deaf, but the technical problems involved are evidently still very great. The authors discuss other applications of the technique covering nearly all fields of sound analysis; linguistic and phonetic investigations, the study of animal calls, the suppression of mechanical noises, and numerous other problems may all benefit. A precise and permanent record that can be investigated at leisure may well provide a better means of classifying and analysing sounds than the rapid and subjective judgment made by listening.

It is evident that the most lavish experimental technique was used to produce that form of display which held out the greatest promise. The authors point out that there is nothing final about the present method, and they refer to some variants of it. But it would have been interesting to hear why a horizontal time scale, a vertical scale for frequency, and an intensity-of-light representation of intensity of sound were chosen throughout all experiments.

THOMAS GOLD.

PRINCIPLES OF SURGERY

Introduction to Surgery. By Virginia Kneeland Frantz, M.D., and Harold Dortic Harvey, M.D. (Pp. 216; illustrated. 12s. 6d.) New York and London: Geoffrey Cumberlege, Oxford University Press. 1946.

The last sentence in this book runs thus: "Whether the student or young surgeon intends to further the cause of surgery as a clinician or as an investigator, a thorough knowledge of the principles included in this small book should help him acquire distinction in his field, extending the achievements of his predecessors." Even without the additional endorsements of such a well-known surgeon as Allen Whipple the candid reader cannot help agreeing with the sentiment expressed in that sentence. The principles of surgery are few, but they need to be inculcated at an early stage of the student's career and thoroughly explained so that he may apply them at every stage of his curriculum and practice. To try to learn surgery without first having a sound knowledge of these principles is to double the labour. Let the young student read, mark, learn, and inwardly digest the contents of this book and he will lay a true foundation for his later work.

After giving that opinion we may perhaps be allowed to point out how the book might be further improved. Though the authors mention syphilis in the description of chronic infections they do not describe the tissue changes in gummatous inflammation; indeed there is nowhere an account of the infecting spirochaete or of the specific cures for the infection. They say that a boil is an abscess centred about a hair follicle, though they explain elsewhere that a slough of dead tissue comes away from it—that is, it is in reality a focus of infective gangrene. There is no mention of postural drainage for an infected knee-joint. In the section on actinomycosis we are told that "if the focus can be completely excised the result is good"; we should not like to deny that, but we can assert that apart from cases of actinomycotic infection of the bowel excision should never be undertaken or considered until penicillin has been thoroughly tried. With these small points of criticism we leave the student to find out the merits of the book for himself.

ZACHARY COPE.

FOUNDATIONS OF NEUROLOGY

Textbook of the Nervous System. A Foundation for Clinical Neurology. By H. Chandler Elliott, M.A., Ph.D. With an Introduction by Wilder Penfield, M.D. (Pp. 384; 158 illustrations, 62 subjects in colour and an atlas. 48s.) Philadelphia and London: J. B. Lippincott Company.

This is a remarkable little book which can be strongly recommended to those who wish to understand the foundations of neurology. The author expresses himself with great clarity, and his ability to simplify difficult facts must subdue the student's usual attitude of despair towards the subject. He explains the anatomical and physiological knowledge on which modern neurology is based in such a way as to rouse the student's interest to study some of the well-selected but not too numerous references given. Furthermore the author shows clearly where our knowledge of function ends and where it is merely groping to correlate a few facts. He gives the reader a balanced outlook which is rarely to be obtained from a textbook. There are many original and ingenious diagrams. For example, in Fig. 91 there is something about the human figure reclining between the red nucleus and the substantia nigra which will provide for most readers an enduring picture of the lamination of the medial lemniscus.

W. RITCHIE RUSSELL.

HANDBOOK OF DERMATOLOGY

Gardiner's Handbook of Skin Diseases. Revised by John Kinnear, O.B.E., T.D., M.D., M.R.C.P.Ed., D.L. Fifth edition. (Pp. 250; 20 coloured plates, 9 from Dufaycolour photographs. 15s.) Edinburgh: E. and S. Livingstone. 1948.

This must be one of the smallest of the many textbooks of dermatology which have appeared in the last half-century, containing as it does only 250 pages. It may well be asked whether this is an important point in its favour or not. Dermatology is a subject which is not well suited to dogmatic discussion. The skin is a very complex organ, and the diseases to which it is subject are so multifarious and so interrelated that an adequate textbook of the subject must contain proper discussion of its problems at such a length that real brevity is necessarily excluded. Probably the original author of this book and his successor have been aware of this consideration but they have kept more in mind the needs of students, who are, as it were, pitchforked into the subject at a certain point of their clinical curriculum and become liable within a few months to satisfy examiners that they have some elementary knowledge of it. Readers in this category when faced with one of the exhaustive manuals of dermatology produced in almost ceaseless profusion by the dermatological specialists of Europe and America are apt merely to be impressed with the difficulty of the subject, to fail to discover any sound principles therein on which to base their own practice, and to be confused by the multiplicity of details. This little book is admirably adapted to the needs of such as these. It is clear, accurate, and brief, and for its size it is very well and amply illustrated.

The introductory chapter is particularly good, and it is gratifying to see that the author draws attention to the complexity of functions undertaken by the skin, a complexity that no doubt accounts for the great variety of the pathological changes to which it is subject. He has brought this edition thoroughly up

to date and discusses well the many advances in therapeutics which we owe to the skill of our chemists and pharmacologists. Perhaps the author might have written rather more extensively on dermatitis and/or eczema, for this is the commonest and most important of all skin diseases now that social education has reformed the habits of the many, and it therefore requires consideration at length even in an elementary textbook. But by and large this is an excellent introduction to dermatology for students, and if they take the trouble to digest its contents during their three months' attendance at the out-patient clinic they will become better and wiser practitioners.

H. HALDIN-DAVIS.

MEDICINE IN GENERAL PRACTICE

Internal Medicine in General Practice. By R. P. McCombs, M.D., F.A.C.P. Second edition. (Pp. 741; 122 illustrations. 42s.) Philadelphia and London: W. B. Saunders Company. 1947.

If it is held that the general practitioner's effective future depends on his capacity to become an efficient general physician then this book surely deserves a welcome. To earn a wide regard, however, such a book must prove that it meets the needs of the family doctor better than do the standard textbooks of medicine here and in the U.S.A. Dr. McCombs can claim this, for his book is a little cheaper and less than half the size (741 pages) of its established rivals. Since it is written by one man it has a uniformity of conception and performance which these other books notably lack; moreover its author seldom loses sight of the whole patient in the enthusiastic concentration upon one part of him. He knows, too, the needs of the family doctor and the errors that may betray him, and the account of each system is preceded by a discussion of symptomatology and diagnostic methods which is altogether admirable. These are great merits, but the book cannot be unreservedly recommended to the British doctor.

The attention given to certain diseases is inadequate; for example, diseases of the nervous system are described in no more than one-eighteenth of the total space—cerebral tumour being dismissed in half a page. While this book has the excellent American practice, now followed in Britain, of giving a relevant bibliography at the end of each chapter, the references are almost exclusively American. It is apparent that a familiarity with the English literature would have led the author to change the presentation of certain sections of the book—as, for example, the accounts of renal disease, heart failure, liver disease, and gastritis. (It is an odd result of the economics of American medicine that in the account of the investigation of gastro-intestinal disorders the author states that "the cost of *x*-ray study precludes its use as a nearly routine measure.")

Finally and most important, a reduction in size of a textbook of medicine must be obtained by the exclusion of material previously regarded as relevant. Dr. McCombs has chosen to omit consideration of the basic sciences, nearly all the pathology, and most of the physiology and anatomy which to-day find their way into the orthodox textbook. The fundamental knowledge, one would surmise, that the family doctor is most in danger of forgetting is thereby excluded. The book is well produced and nicely written, it is accurate and its information is up-to-the-minute (there are accounts of streptomycin, nitrogen mustard, folic acid, radioactive iodine, and cytochrome-C), but it must be judged to fail not in its execution but in the initial misconception of its purpose.

D. V. HUBBLE.

It has been said that a medical student must learn the equivalent of a foreign language in order to master sufficient of the nomenclature needed to understand medical works, and all medical men no doubt pay some attention, if only fleeting, to the structure of our terminology. Perhaps we are not critical enough, else why should we accept such peculiarities as "antibiotic" and "deratization" so easily? Mr. Peter D. Ridge-Beedle, in *Why Not English?* (Stratford Press, 10s. 6d.), criticizes another aspect of the English language—its spelling—and propounds a reformed system that necessitates 42 letters in all. The author's system is not itself consistently phonetic, for he uses the same sign "r" for the "er" sound of "father" and the "r" sound in "rough." The obstacle of varying pronunciation appears in his spelling of the word "language," the last syllable of which he treats as if it rhymed with "age," whereas many would rhyme it with "midge."

BOOKS RECEIVED

[*Review is not precluded by notice here of books recently received*]

Vitamine und Vitamintherapie. By E. Abderhalden and G. Mouriquand. (Pp. 408. 28 Swiss francs.) Berne: Huber. 1948.

A general account of clinical and experimental work on the vitamins.

Endocrinology of Neoplastic Diseases. Edited by G. H. Twombly, M.D., and G. T. Pack, M.D. (Pp. 392. 60s.) London: Geoffrey Cumberlege. 1947.

A collection of papers by various American authorities.

Pathological Processes in Malaria and Blackwater Fever. By B. Maegraith, M.A., M.B., D.Phil., B.Sc. (Pp. 430. 35s.) Oxford: Blackwell. 1948.

An account of the clinical and pathological aspects of malaria and blackwater fever, with references.

Myotonia. By E. Thomasen. (Pp. 251. 20s.) London: H. K. Lewis. 1948.

A monograph on the clinical aspects, treatment, and inheritance of the myotonias.

Eat and be Healthy. By L. Nicholls, M.D. (Pp. 56. 4s. 6d.) London: Associated Newspapers of Ceylon. 1948.

Instruction on sound diet for the layman in Ceylon.

Hodgkin's Disease and Allied Disorders. By H. Jackson, Jr., A.B., M.D., and F. Parker, Jr., A.B., M.D. (Pp. 177. 45s.) London: Geoffrey Cumberlege. 1947.

An account of the pathology, symptomatology, and treatment.

Aids to Organic Chemistry. By S. F. Smith, M.B., B.S. 3rd ed. (Pp. 127. 4s. 6d.) London: Baillière, Tindall and Cox. 1948.

Intended for medical students.

Die Morphogenese der Hypertrophie und des Karzinoms der Prostata und ihre Bedeutung für die Klinik. By R. Howald. (Pp. 40. 4 Swiss francs.) Basle: Schwabe. 1948.

A monograph on prostatic hypertrophy and carcinoma, with photomicrographs.

Veterinary Protozoology. By U. F. Richardson, B.Sc., M.R.C.V.S. (Pp. 240. 18s.) London: Oliver. 1948.

An account of the protozoa that attack animals, particularly in the Tropics.

Plant Viruses. By K. M. Smith, F.R.S. (Pp. 78. 6s.) London: Methuen. 1948.

An introduction for the botany student or general reader.

La Mortalité de L'Enfant de Première Année. By C. Candiotti and C. Moine. (Pp. 64. No price.) Paris: Baillière. 1948.

A monograph on infantile mortality in France.

A Primer in Clinical Science. By R. D. Wright. (Pp. 43. 3s. 6d.) London: Melbourne and Oxford University Presses. 1948.

An introduction to clinical work for the student.

Jaundice: Its Pathogenesis and Differential Diagnosis. By E. R. Movitt, M.D. (Pp. 261. 42s.) London: Geoffrey Cumberlege. 1947.

A practical manual for the clinician; with bibliographies.

The Use of Isotopes in Biology and Medicine. By H. T. Clarke and others. (Pp. 445. $5.00.) Madison: Wisconsin Press. 1948.

A symposium on the use of isotopes in research.

Recherches Personnelles pour Servir à L'Étude de la Gonococcie. By A. Guépin. (Pp. 218. No price.) Paris: Presses Universitaires. 1933.

An account of the author's experience in treating gonorrhoea.

Research Reports. Feeding Problems in Man as Related to Environment. By R. E. Johnson, M.D., D.Phil., and R. M. Kark, M.R.C.P. (Pp. 94. No price.) Chicago: U.S. Army Medical Nutrition Laboratory. 1947.

An analysis of U.S. and Canadian army ration trials and surveys during the recent war.

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WORLD HEALTH ORGANIZATION

The World Health Assembly of the World Health Organization concluded its first meeting on July 24 after being in session for a month, during which the various committees (each a committee of the whole) were unremitting in their attention to the problems before them. Sixty-eight nations were represented by delegates and observers on this historic occasion, and the first meeting of the World Health Assembly provided a notable illustration of the well-worn saying that medicine knows no frontiers. The remarkable measure of agreement reached and the spirit of co-operation displayed were in no small part due to the skill and tact with which the President of the Assembly, Dr. Andrija Stampar, of Yugoslavia, conducted its deliberations; and, also in no small part, to the efficiency of the secretariat under Dr. G. Brock Chisholm, newly appointed Director-General of WHO, who for the past two years has been acting as Executive Secretary to the Interim Commission. The work of the Assembly completed, the first meeting of the Executive Board was held, with Dr. A. T. Shousha Pasha as Chairman and Dr. K. Evang and Dr. W. W. Jung as Vice-chairmen. The immediate problem before WHO is the establishment of a permanent central staff under the Director-General and the setting on foot of projects considered to be urgent. It is expected that the Executive Board will meet in the autumn, when its eighteen members (representing eighteen States) will have had the opportunity to consider at greater leisure the numerous matters discussed in June and July. The first legislative act by WHO has already been performed by the issue of regulations laying down detailed methods of procedure to be used by the various member countries in the compilation of data on diseases and causes of death.

It will naturally take a little time before the central staff at Geneva finds its working feet, and it is therefore in some ways a pity that five of the regional organizations are to be set up before the central administration is firmly established. The six regions into which for the purposes of WHO the world is to be divided are: European, Eastern Mediterranean, South-East Asian, Western Pacific, African, and North and South American. The last named has of course been admirably served for years by the Pan-American Sanitary Bureau, and negotiations are on foot for its integration in WHO. The desire to establish quickly offices in the other five regions is understandable, and with the good will displayed by the member States in the World Health Assembly difficulties that may arise should be easily solved. But the project which WHO has in hand is so tremendous in its implications that it would be a mistake if the desire to get something done speedily for reasons of prestige or justification were to encourage initial imperfection of organization. The plans for the work of WHO must of necessity be worked out from year to year and framed in accordance with its annual budget. But it is not fanciful to suggest that the ideal that it has set itself would need a long-term policy conceived in terms of decades rather than calendar or financial years. It would seem, therefore, of the first importance that the foundations of its central and regional organizations should be laid with the utmost care if the structure to be raised upon them is to be adequate to the high purpose WHO has set itself of "the attainment by all peoples of the highest possible level of health."

To begin the first year of work of WHO the Interim Commission had proposed a budget of $6,500,000 for 1949, and a decision to cut this to $5,000,000 (about £1,250,000) came as a disappointment to many. It certainly seems a small enough budget with which to start health activities on a world-wide scale. Nevertheless, the expenditure of the United Nations and its specialized agencies amounts in all to a vast annual sum, about half of it being contributed by the U.S.A. The sceptic might reflect that if the money spent by the United Nations was put at the disposal of WHO, in exchange for WHO's budget of $5,000,000, the world would be a healthier and happier place to live in. But discarding this proposition as Utopian, we may believe WHO will find it will achieve concrete results by having to concentrate on carefully selected programmes of manageable dimensions. The six principal health problems it has decided to tackle in 1949 are: malaria, tuberculosis, venereal disease, maternal and child health, nutrition, and environmental hygiene. These are matters which call for five- or ten-year plans, and even then so much depends upon the social and economic conditions, sanitation, personal and communal habits of different peoples that the success of an attack upon, for example, tuberculosis will reside as much in the solution of these as in preventive and curative measures. Granted peace, improved sanitation in backward areas, the alleviation of social and economic distress, there yet remains the provision of enough well-trained doctors and nurses and all the other skilled equipment of modern medicine. Beyond this there is the inculcation among peoples of the principles of health and hygiene. Many of these things are in the control of forces outside the world of medicine, but medicine has one potent instrument which it can put at the disposal of regions less favourably placed than, say, the U.S.A.—and that is expert knowledge. WHO should be a power-house of information on all those matters which come within its purview, and the insistence of many delegates at Geneva on the importance of the editorial and publications services of WHO showed their live awareness of this fact.

It may be pertinent here to trace the development of the idea of the international control of disease, which has now progressed to the idea of the international promotion of health. Quarantine as a protection against plague was introduced into the Mediterranean in the fourteenth century, the inspiration for this coming from the observations on leprosy in Leviticus. And similar action was taken in North America in 1647 against the fever (yellow fever) in Barbados. The spread of Asiatic cholera across Europe in the first half of the last century reminded Europe once

more that infectious agents are indeed international, and a formal international sanitary convention was drawn up at a meeting of the International Sanitary Conference in Venice in 1892.[1] The first health agency to operate for several Governments was, however, the Pan-American Sanitary Bureau, established at a conference at Washington in 1902. In 1909 the Office International d'Hygiène Publique (OIHP) was set up in Paris, and operated until 1946, when the decision was taken to amalgamate it with WHO. With the appearance of the League of Nations after the war of 1914–18 it was proposed to place international health bureaux under the authority of the League, but the OIHP continued its separate existence in a compromise arrangement with the Health Organization of the League—an organization which represented the one solid contribution the League made to human welfare. The war of 1939–45 naturally interfered with the work of OIHP and the League Health Organization, and the gap was temporarily filled by Unrra, whose activities ended in December, 1946, in Europe, and in March, 1947, in the Far East, some of its functions being transferred to the Interim Commission of WHO. The project of a new and comprehensive health organization was discussed at the United Nations conference in San Francisco in 1945, and in February, 1946, the Economic and Social Council of the United Nations set up a technical preparatory committee, which shortly after prepared draft constitutions for a world health organization. The next step was the holding of the International Health Conference in New York in June, 1946, when the constitution of WHO was signed by representatives of 61 States. The constitution was to come into force when 26 members of the United Nations had ratified their signatures, and the Interim Commission of 18 States undertook the preparatory work of establishment until ratification; it also continued the functions of former international health organizations and the consideration of urgent health problems. It was expected that the Interim Commission would have a life of only a few months, but this, in fact, was prolonged for about two years, ending with the official birth of WHO in April of this year.

There is not space here to enumerate the various activities of WHO.IC during the past two years. We may note the completion of the Sixth Decennial Revision of the International Lists of Diseases and Causes of Death, the appointment of an expert committee on malaria, the extension of work on biological standardization, field services in epidemiology, the provision of travelling fellowships, work on an international pharmacopoeia, and in particular the emergency committee established during the cholera epidemic in Egypt in the autumn of 1947.

The conception of WHO is one that should appeal to the imagination, and indeed it will call for imagination on the part of those directing its activities if its work is not to be hampered by the natural defence mechanisms of bureaucracy. In full recognition of the great progress already made we may suggest that one of the problems of WHO will be to keep its organization flexible and of such a size that the Director-General will be able to remain in close touch with his staff. In a recent broadcast Sir Lawrence Bragg observed that when an institution grew beyond a certain size its director—he was of course referring especially to research—lost that close touch with his subordinates which made for efficient and productive team work. Establishments have a natural tendency to grow, but it is to be hoped that the number of permanent officials in WHO will be small enough for the Director-General through personal contact with each one to take that close interest in their work which is essential if an institution is to be something a bit more than an efficient organization.

[1] For this and other information see *Official Records of the World Health Organization*, No. 9.

MEDICAL AND SCIENTIFIC INFORMATION

The burden of the printed word to-day lies heavily on the world of science, an inevitable outcome of the great volume of research work carried out in the laboratories of pure and applied science in the universities, research institutes, and industrial organizations of so many countries. Our civilization is no longer one based on the humane studies, pervaded as it was with a sense of leisure and free from obsession with the time-table. We live in a technological age when the speed of discovery and the application of what is discovered bring with them a sense of impermanence and insecurity. The unceasing accumulation of facts daunts even the most comprehensive mind, and man's capacity for analysis far outstrips his ability to provide a synthesis. The man of science who contributes to knowledge finds himself working in ever-narrowing fields of inquiry, so intense has specialization become. The spate of publications makes it increasingly difficult for him to know what workers in adjacent fields are doing. "As a result," to quote from a document issued by the Royal Society for its Scientific Information Conference in June, "the task of keeping up with scientific literature is becoming an impossible one, and is in turn leading to inefficiency and to a certain amount of frustration in scientific research and in the application of science." The Royal Society has once more put the world of learning in its debt by holding such a conference, which was attended by delegates from the Dominions and other countries.

Unfortunately its meeting coincided with the Annual Meeting of the B.M.A. at Cambridge, but the B.M.A. was represented by the Editor of its two abstracting journals, Dr. G. M. Findlay, and by Professor Samson Wright. The Conference tackled through four sections the following problems: "(1) Publishing and distributing original scientific papers. (2) Issuing and using abstracts to convey current awareness of availability and relevance of such papers. (3) Consolidating abstracts or other forms of reference into continuously cumulative indexes and using these and other library services for the retrospective searching of the literature. (4) Producing and utilizing periodical reviews of progress in designated fields of science." A number of valuable notes and memoranda were made available. If scientific knowledge is becoming unmanageable it is interesting to note that the science of documentation is providing methods to keep pace with it. Most are familiar with the use of the photostat and microfilm, but new to many will be the Dutch invention whereby "a foolscap page can

be reproduced within the dot of a letter 'i,' or the whole of the *Encyclopaedia Britannica* on three quarto pages." This method enables very minute microphotographic images, legible through a microscope, to be printed on a paper base. Another Dutch invention uses diazo instead of silver chemicals for reproduction by reflex photography. New mechanical methods may revolutionize the method of presenting and distributing information and may yet be linked up with Professor J. D. Bernal's proposals for distributing scientific papers, the value of which was somewhat obscured by the controversy surrounding it at the outcome of the Conference.

Whatever direction future developments may take, abstracts of current scientific literature will become of increasing importance. The medical man who does research work is under the same pressure of specialization as other workers in science. There is hardly any field of medicine in which the observations and methods of the pure sciences do not find some point of application. The clinician who specializes tends to do so at the expense of his knowledge of medicine as a whole. To provide a synoptic view of medicine is the aim of *Abstracts of World Medicine*, and *Abstracts of World Surgery, Obstetrics and Gynaecology*. In his editorial notes for the Royal Society Conference, Sir David Chadwick observed that "the indefinite multiplication of largely unrelated abstracting agencies and of abstracts journals is not, however, a good solution"—an observation made under the heading of "Promptness in Issue of Abstracts." To grapple with this question in Medicine Unesco has during the past eighteen months[1] set up an Interim Co-ordinating Committee on Medical and Biological Abstracting in Paris to examine the situation and to look into possible ways of collaboration among existing medical abstracting agencies. The outcome of its penultimate meeting was discussed in a leading article in the *Journal* of Oct. 11, 1947. The preliminary survey thus made was thought by the General Assembly of Unesco to justify the setting up of a co-ordinating committee in medical abstracts under the aegis of Unesco, whose function is that of convener and secretariat. At a meeting in Paris in April of this year under the chairmanship of the Editor of the *British Medical Journal* the matter was carried a stage further in a two-day conference in which representatives of the following organizations took part: *Abstracts of World Medicine; British Abstracts; Excerpta Medica;* International Federation for Documentation; Medical Library Association, U.S.A.; and the International Federation of Library Associations. In addition to representatives of the above as members of the Committee, the United Nations, the World Health Organization, *Chemical Abstracts*, and Ingeniors Vetenskaps Akadmien (Stockholm) sent observers who made valuable contributions to the conference. The meeting was organized by the Natural Sciences Division of Unesco under its director, Dr. Joseph Needham, and the Medical Counsellor of the Division, Dr. I. M. Zhukova. The meeting in April was of value in that those with expert knowledge of various aspects of documentation were able to pool their information and exchange ideas on what on the surface would appear to be a somewhat dull subject but is far from being so. Towards the end of the meeting it became clear that there was enough useful and indeed urgent work to be done on the subject of medical abstracting to justify dropping the word "Interim" from the title of the Committee if other organizations see fit to become members of it. It was resolved, for example, that WHO and FAO should join Unesco in sponsoring the activities of this Committee, and this WHO has now agreed to do. Invitations have been sent to other abstracting agencies to join in the work of co-ordination, and it is hoped that a full meeting will be held in the early part of next year.

In a world which modern transport has reduced to a manageable unit of travel and communication the specialized agencies of the United Nations—Unesco, WHO, and FAO—have a greater chance of promoting international understanding than the parent world organization. If there had been any suspicion that Unesco was merely pursuing an academic exercise in seeking to co-ordinate the activities of medical abstracting this should have been removed by the stress laid upon this kind of work by the Royal Society conference in June. To translate discussion into action will be the problem of the Co-ordinating Committee on Medical and Biological Abstracting in its future conferences.

[1] *British Medical Journal*, 1946, **2**, 378.

NITROGEN MUSTARD

The therapeutic development of the nitrogen mustards or alkylamines is an example of the beating of swords into ploughshares; for it was following the observation of the effects of mustard gas on the haemopoietic tissues that the nitrogen compounds came to be employed in the treatment of Hodgkin's disease, leukaemia, and allied disorders. We publish elsewhere in this issue a paper by Dr. D. C. Sinclair on mustard-gas poisoning. Much of the experimental work with this substance could not be published at the time it was undertaken, and it is now evident that "security" robbed Dr. J. F. Wilkinson[1] and his colleagues in Manchester of priority in describing the therapeutic use of the nitrogen mustards, since their results were available to the American workers[2 3 4] in the same field who are generally given the credit for introducing these new drugs.

The two compounds used have been methyl-bis(β-chloroethyl)amine hydrochloride and tris(β-chloroethyl) amine hydrochloride. Both these substances are readily soluble in water, in which they rapidly undergo chemical rearrangement, forming first cyclic ethylene-imonium derivatives with powerful effects on mitosis and intracellular enzyme systems, and later other relatively inactive compounds. Most workers have used the "bis" compound, but there is no significant difference between the effects of the two. The initial dose has usually been 0.1 mg. per kg. of body weight, repeated on consecutive or alternate days until three to six doses have been given. It is administered intravenously, with precautions to avoid leakage into the subcutaneous tissues, for the nitrogen mustards retain the vesicant properties of mustard gas. Nausea and vomiting three or four hours after injection almost always

[1] *Lancet*, 1947, **2**, 540.
[2] Gilman, A., and Philips, F. S., *Science*, 1946, **103**, 409.
[3] Goodman, L. S., Wintrobe, M. W., Damashek, W., Goodman, M. J., Gilman, A., and McLennan, M. T., *J. Amer. med. Ass.*, 1946, **132**, 126.
[4] Jacobson, L. O., Spurr, C. L., Barron, E. S. G., Smith, T., Lushbaugh, C., and Dick, G. F., *ibid.*, 1946, **132**, 263.
[5] ApThomas, M. I. R., and Cullumbine, H., *Lancet*, 1947, **1**, 899.
[6] Wintrobe, M. W., Huguley, C. M., McLennan, M. T., and Lima, L. P. de C., *Ann. intern. Med.*, 1947, **27**, 529.
[7] Chevallier, P., Lamotte, S. ,Brion, S., and Sabouraud, *Sang*, 1948, **19**, 97.
[8] *Blood*, 1947, **2**, 564.

occur; anorexia and headache are common during the three or four days of the drug's administration. The effect on haemopoiesis is apparent within two to five days and is commonly greatest by the 18th day after injection. The total leucocyte count falls in every instance; the first change is a lymphopenia, and this is rapidly followed by a neutropenia. With the doses in common use it is unusual for the leucopenia to be less than 2,000 per c.mm., and a true agranulocytic syndrome occurs in less than 1%. Thrombocytopenia is less frequent, and the count seldom falls below 60,000 per c.mm.; but transient purpura has been noted. The effect on the erythrocyte count is variable and usually insignificant.

The therapeutic activity of the alkylamines has now been studied in a number of the proliferative and neoplastic diseases of haemopoietic tissue, and it is justifiable to attempt some assessment of their value. There is a remarkable unanimity in the numerous reports available.[5 6 7] Hodgkin's disease responds satisfactorily, and remissions lasting several months have followed a single course of injections, but they are usually shorter than after irradiation. Most workers have been impressed with the improvement shown by some patients in the stage of terminal cachexia and with the rapid relief of pain due to skeletal infiltrations. Nevertheless the alkylamines will not cure Hodgkin's disease, nor do they appear to be in general as effective as radiotherapy. In the related disorders the results are less satisfactory, but chronic myeloid leukaemia can often be controlled, and in the other reticuloses and in reticulosarcoma temporary improvement was sometimes seen. In myelomatosis and most epithelial neoplasms the results were bad, though occasionally patients with bronchial carcinoma have improved remarkably. Remissions were obtained in a proportion of patients with polycythaemia vera. An unsatisfactory result in a case of this disease is described by Dr. A. W. Woodruff on page 299 in this issue. The initial fall in red blood cells was considerable, but thereafter the tendency to rise again was not controlled by further treatment. Mycosis fungoides varies in its response; most workers report indifferent results, but Henstell, Tober, and Newman[8] recorded immediate and striking remissions in six patients. They found that nitrogen mustard was most successful when reticulum cells dominated the cutaneous infiltrations, and they concluded that the drug had a selective action on this cell.

The importance of the nitrogen mustards lies not in their immediate therapeutic application but in the discovery of a group of chemical substances which have a lethal action confined to one particular type of cell. It is possible that more powerful and more specific drugs will become available, since numerous compounds related to the nitrogen mustards could be synthesized and given clinical trial.

LIVE AND DEAD YEAST

The value of dried autolysed yeast as a source of some members of the vitamin-B complex is undoubted, and this material has been widely used by patients with symptoms of chronic vitamin deficiency. However, the usefulness of live yeast has not been so certain, and a group of workers[1 2] at Wisconsin University have recently obtained very different results with live and dead yeasts. In a series of experiments they found that the addition of up to 150 g. daily of fresh yeast to the diet of normal individuals did not have the expected effect of increasing the urinary excretion of riboflavin, and that in the case of vitamin B_1 the urinary excretion actually decreased. Analysis of the faeces showed that the vitamins had not been absorbed. The same results were obtained with three types of dried yeast which still retained life. Only dead yeast was found to increase the urinary excretion of riboflavin and aneurin. The conclusions drawn from these results are first that live yeast, though containing a large concentration of vitamin B_1 and riboflavin, is not in practice a good source of these vitamins, since they cannot be absorbed from the living cells, and therefore pass into the faeces; secondly, the living yeast appears actively to compete in the gut for such other vitamin B_1 as is available, and so actually reduces the amount that might be absorbed.

These results, if they remain undisputed, serve to point out the complexity of the factors which may affect the nutritional status of a patient. It is now realized, for example, that the requirement of a particular vitamin may vary with the quantity and quality of protein in the diet; indeed it seems likely that nicotinic acid is not needed at all if the diet contains sufficient tryptophan. Again, the microbiological synthesis of vitamins in the intestinal tract may be a significant source for man as well as for the ruminants. In the light of all these findings the too rigid use of tables of vitamin requirements and food contents seems unjustified.

[1] Price, E. L., Marquette, M. M., and Parsons, H. T., *J. Nutrit.*, 1947, **34**, 311.
[2] Kingsley, H. N., and Parsons, H. T., ibid., 1947, **34**, 321.

TREATMENT OF TYPHOID CARRIERS

The typhoid bacillus was formerly classed as a penicillin-resistant organism, but it is in fact the least resistant of the intestinal pathogens and must be classed among the bacteria which, in theory at least, can be successfully attacked with high concentrations of the drug. R. W. Evans[1] examined 66 strains and found that the concentration required to inhibit growth completely varied from over 25 (in only 1 strain) to 10 units per ml., which inhibited the majority. Lower concentrations retarded the growth of many strains, and sensitivity was unrelated to phage type. J. W. Bigger[2] was the first to show that sulphathiazole acts synergically with penicillin on *Salm. typhi*; this action was studied and confirmed by G. T. Stewart[3] and by J. C. Thomas and W. Hayes,[4] whose elaborate experiments took into account every possible variable and fully confirmed previous belief that concentrations of the two drugs which are attainable therapeutically in certain situations should have a marked effect. Bigger's observations led directly to a trial by C. J. McSweeney[5] of the action of the two drugs in combination on typhoid fever; he reported very favourable results in six cases. The treatment was vigorous, penicillin being given at only two-hour intervals in doses of 200,000 units and sulphathiazole at the rate of 1g. three hourly for periods of four days. Trials of this form of treatment in several Army Commands, reported by C. G. Parsons,[6] did not confirm the favourable impression formed in Ireland, but it is to be noted that McSweeney's treatment schedule was not exactly followed; in particular the interval between penicillin injections was longer in almost all cases, and, since the maintenance of a high concentration is obviously desirable, this may have been an important factor.

The possibility that typhoid carriers might be cured by this treatment has not been overlooked, but hitherto no adequate series of such cases has been studied. On page 295 of this issue R. M. Fry and his colleagues now report such a series. They studied the *in vitro* sensitivity of the strains of *Salm. typhi* concerned to the two drugs separately and in combination, and, though the evidence of synergic effect

[1] *Lancet*, 1946, **2**, 113.
[2] Ibid., 1946, **1**, 83.
[3] *J. Hyg.*, 1947, **45**, 282.
[4] Ibid., 1947, **45**, 313.
[5] *Lancet*, 1946, **2**, 114.
[6] Ibid., 1948, **1**, 510.

is perhaps less striking than that afforded by the experiments of Thomas and Hayes, it is sufficient to encourage hopes of effective *in vivo* action from large doses. They also confirmed that penicillin given in large doses intramuscularly is excreted in considerable concentration in the bile. Nevertheless the treatment of seventeen persistent carriers with penicillin and sulphathiazole gave singularly disappointing results. Three systems of treatment were tried employing progressively huger doses of penicillin, culminating in 40 million units of penicillin together with 12 g. of sulphathiazole daily. Courses of both continuous and intermittent treatment were given. The net result was the apparent cure of only three of the seventeen patients. This is certainly not encouraging, and further search must be made for some chemotherapeutic procedure which will deal more successfully with these patients. It would be a mistake to interpret the results as evidence against the efficacy of these drugs in typhoid fever itself. To eliminate an organism from the body altogether is a far more difficult task than to suppress its activity sufficiently to alleviate an acute infection. There are other infections, notably streptococcal, of which the acute form is highly susceptible to chemotherapy while the carrier state is often resistant.

THE REFLECTING MICROSCOPE

The action of the Nuffield Trustees in making a grant to the University of Bristol for the construction and development of the reflecting microscope designed by Dr. C. R. Burch, of the Department of Physics of that University, is an indication of the potential value in research of this appliance. At the recent exhibition in London arranged by the Physical Society Dr. Burch and his co-workers described some of the uses to which the reflecting microscope may be put. It is not to be supposed that the normal refracting microscope is in danger of being supplanted. Difficult technical procedures, including the precision testing and polishing of aspherical surfaces, will limit the production of the reflecting type of instrument, and it may be expected that its uses will be confined to those in which it offers specific advantages. One of these is a substantial increase in working distance. The existing reflecting instruments have a numerical aperture of 0.98 with oil immersion and 0.65 without. Yet the working distance can be 14 to 20 mm. This is of obvious convenience in micromanipulation, which is a sufficiently difficult technique without the further handicap of the more restricted working distance imposed by a refracting microscope of high magnification. In metallurgical research the increased working distance permits the examination of the surface changes which take place in alloys at temperatures up to red heat and somewhat beyond.

The second main advantage arises from the fact that the optical properties of a mirror system are independent of wavelength. Dr. R. Barer, of the Department of Anatomy and Physiology at Oxford, has been examining this aspect of the reflecting microscope, and though his work is still at an early stage sufficient has been done to indicate the technical possibilities of the method. One series of measurements has been on the absorption profile of a red cell over a range of wavelengths extending well into the ultra-violet. For this purpose there is a substantial advantage in a system which can be operated over a continuous range of wavelengths. The reflecting microscope can be used with shorter wavelengths than a refracting ultra-violet microscope. To what extent this may be an advantage for the normal purposes of microscopy must be a matter of opinion. There are those who consider that the probability that changes will be produced in the material under examination—or, as such critics would say, under bombardment—outweighs the advantage of greater resolution from shorter wavelengths. The instrument should not, in any case, be regarded as rendering obsolete the refracting type of ultra-violet microscope, of which a new British representative was shown at the Physical Society's exhibition. The two should rather be regarded as complementary. In biological research the reflecting microscope is likely to be particularly useful for measuring selective absorption, as, for example, in the study of carcinogenetic substances.

The immediate programme is for the production of ten reflecting microscopes of the existing type, and as a long-term project for the development of an instrument with the highest possible aperture. This will involve the use of two aspherical surfaces instead of one in the objective. If reflection is also employed in the condensing system four aspherical surfaces will be required. This is no easy programme, for with more than one aspherical surface axial alignment must present greater difficulty. None the less it is hoped that a numerical aperture in the neighbourhood of 1.4 may be attainable.

VASCULAR CHANGES IN SILICOSIS

The effect of silicosis on the pulmonary circulation is a subject on which there have been differences of opinion, and a study made by Geever[1] on the pulmonary vascular lesions and related pathological changes in 43 cases of silicosis is, therefore, of interest. The cases were unselected and consecutive, but were uncomplicated by gross pulmonary tuberculosis; they were compared with a similar control group of men over the age of 50. The author prepared sections of 40 pulmonary vessels of all sizes from each case, and he classified the silicosis into discrete nodular and massive conglomerate nodular forms. In the discrete nodular form the vascular lesions were not prominent and were found mostly in the arterioles, venules, and capillaries; whereas in the massive conglomerate form the vascular lesions were severe and were found in vessels of all sizes. These findings agree with those of the French school led by Policard,[2] which up to the present has done most work on this aspect of silicotic pathology. Fibroblastic proliferation is the first reaction in all layers of the arterial wall, followed by proliferation of capillary channels and degeneration of muscle and elastic tissue. The final result is occlusion and disruption of the vascular wall by infiltrating granulation tissue, which invades all the layers. Sometimes even thrombosis of large arteries occurs.

In 26 out of the 43 cases right ventricular hypertrophy was found; and in 11 of the 23 patients with massive conglomerate disease failure of the right heart occurred. These findings confirm the physiological observations of Cournand[3] and his colleagues, who showed that pulmonary arterial hypertension existed in two out of the three silicotic patients whom they studied.

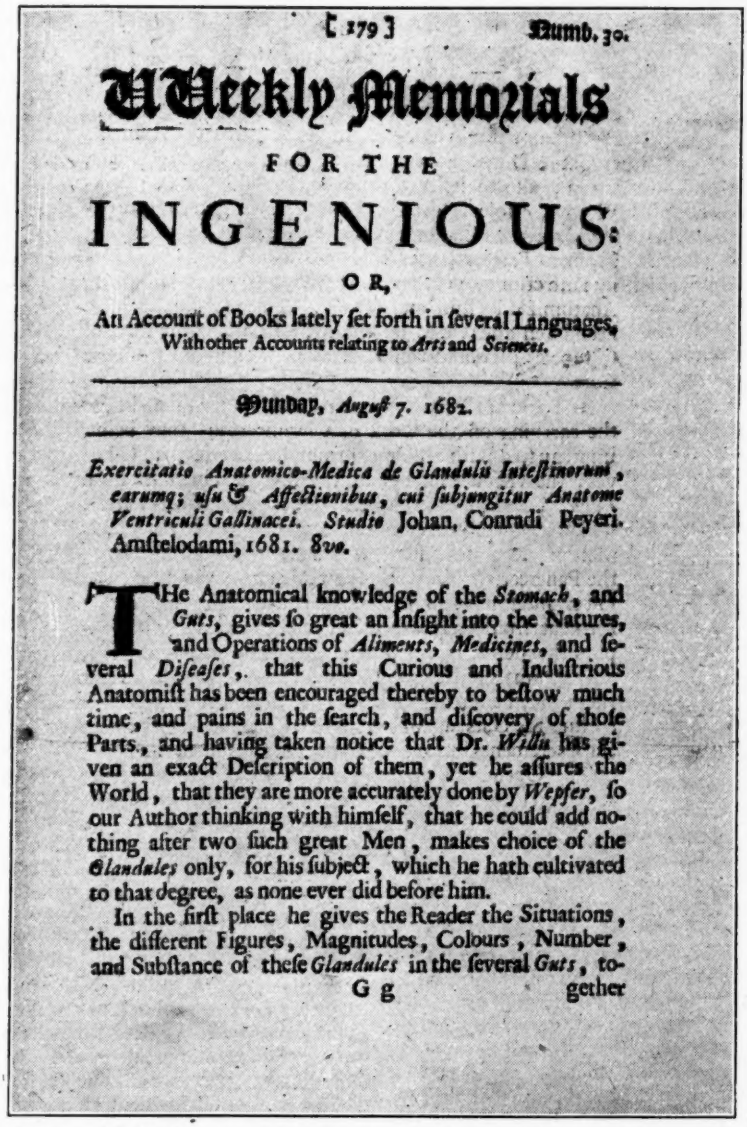
These vascular changes are also important, because they probably are partly responsible for cavity formation. Gough[4] has shown in his lung sections that areas of progressive massive fibrosis in South Wales coal-miners frequently have a central cavity. Gardner,[5] while discussing pneumoconiosis of all types, mentioned anaemic necrosis as a cause of the irregular slit-like cavities which are found in silicotic fibrous masses, and Vorwald[6] also considered that the cavitation which occurred in conglomerate nodular fibrosis was secondary to interference with the blood supply.

[1] *Amer. J. med. Sci.*, 1947, **214**, 292.
[2] *Ann. Anat. path. méd.-chir.*, 1939, **16**, 97.
[3] *J. clin. Invest.*, 1946, **25**, 639.
[4] *Occup. Med.*, 1947, **4**, 86.
[5] *J. Amer. med. Ass.*, 1940, **114**, 535.
[6] *Amer. J. Path.*, 1941, **17**, 709.

Nova et Vetera

THE FIRST ENGLISH MEDICAL JOURNAL

It has been stated[1] that the first English medical journal was the *Medicina Curiosa*, only two numbers of which were published—in June and October, 1684. This claim has never been challenged, and if the term "medical journal" is taken to mean a periodical devoted exclusively to medicine, then the *Medicina Curiosa* has no rival. It is not, however, the first English journal dealing with medicine. Two and a half years earlier, on Jan. 16, 1682, there was published the first number of what is undoubtedly the first English abstracting journal, and at least one-third of its space was given up to accounts of medical books and papers. This journal is now very rare and appears to have been overlooked by the medical historian (it is not mentioned even in Garrison's comprehensive list of seventeenth- and eighteenth-century medical and scientific periodicals[2]), yet the quantity and importance of its medical contributions far exceed those of the *Medicina Curiosa*.



[179] Numb. 30.

UWeekly Memorials

FOR THE

INGENIOUS:

OR,

An Account of Books lately set forth in several Languages, With other Accounts relating to *Arts* and *Sciences*.

Munday, *August* 7. 1682.

Exercitatio Anatomico-Medica de Glandulis Intestinorum, earumq; usu & Affectionibus, cui subjungitur Anatome Ventriculi Gallinacei. Studio Johan. Conradi Peyeri. Amstelodami, 1681. 8vo.

THe Anatomical knowledge of the *Stomach*, and *Guts*, gives so great an Insight into the Natures, and Operations of *Aliments*, *Medicines*, and several *Diseases*, that this Curious and Industrious Anatomist has been encouraged thereby to bestow much time, and pains in the search, and discovery of those Parts, and having taken notice that Dr. *Willis* has given an exact Description of them, yet he assures the World, that they are more accurately done by *Wepfer*, so our Author thinking with himself, that he could add nothing after two such great Men, makes choice of the *Glandules* only, for his subject, which he hath cultivated to that degree, as none ever did before him.

In the first place he gives the Reader the Situations, the different Figures, Magnitudes, Colours, Number, and Substance of these *Glandules* in the several *Guts*, together

Gg

No. 30, with the first account in English of "Peyer's patches." (By courtesy of the Wellcome Historical Medical Museum.)

It appeared with the captivating title *Weekly Memorials for the Ingenious: or, An Account of Books lately set forth in several Languages, With some other curious novelties relating to Arts and Sciences*. Each number consisted of eight small quarto pages, and its object was clearly stated in the preface to the first number.

"I cannot doubt but that this weekly paper will find a candid and cheerful acceptance amongst all ingenious persons; the design of it being to present them with a short view of the worthy Labours daily set forth by the Learned. The bare Titles of Books yearly printed in our Common Catalogues, are somewhat dry things, scarce able to raise in men that gust and appetite to Learning, which we may hope these brief Accounts will give them. I shall not confine my self in my Undertaking onely to Authors of our own Nation, but shall likewise give Accounts of most Books transmitted to us from all other parts; and shall transcribe here as most valuable, as well in reference to Accounts of Books, as to other curious Novelties therein contained; and of these I may in time communicate what I may receive from elsewhere."

The anonymous writer of this preface was thought to be a certain Mr. Beaumont, who, after the appearance of nine consecutive numbers, quarrelled with his publishers, Henry Faithorne and John Kersey, and on March 20 began to produce a rival journal with an identical title which was published by R. Chiswel, W. Crook, and S. Crouch. Undeterred, the original publishers carried on with their project until the end of the year and produced fifty consecutive numbers. Beaumont's rival weekly expired after the twenty-ninth number.

The editor of the modern abstract journal, surveying the ever-growing mass of medical and scientific periodical literature, must envy the leisurely task of his seventeenth-century forerunner. There were few journals of any kind in Europe at that time. The *Journal des Scavans*, first published in January, 1665, anticipating the *Philosophical Transactions* of our own Royal Society by three months, was the first scientific journal in any modern European language. Nicolas de Blegny's *Nouvelles Descouvertes* (1679) was the first medical journal in the vernacular.[3] The well-known *Acta Eruditorum* did not begin until 1682. Abstracts of papers appearing in these journals were printed in the *Weekly Memorials*, but books were still the chief source of up-to-date information, and substantial abstracts of important medical books form the chief item in many numbers. The greater part of Nos. 4 and 7 is taken up by an abstract of the first volume of de Blegny's journal, in the Latin translation made by Théophile Bonet and published at Geneva in 1680 with the title *Zodiacus Medico-Gallicus*. No. 6 contains an account of a work by John Collins (London, 1682) on salt and its use in food-preserving, and a description of "The Physick of the Americans of Virginia" from the *Journal des Scavans*. *The Observationes Physico-Medicae*, of Johann Hellwig is summarized in No. 9, and a fortnight later the place of honour is given to a report of the biochemical and pharmaceutical experiments described in J. H. Juncken's *Chymia experimentalis Curiosa*, an account which is continued in No. 15. The inaugural dissertation of G. W. Wedel on arthritis is noticed in April, and an account of the same author's book on setons, or "artificial issues"—then popular as a preventive against plague and fever—occupies a half of the number for May 22. One of the most interesting seventeenth-century accounts of the Chinese system of medicine, especially of the pulse theory, was the *Specimen Medicinae Sinicae*, by Andreas Cleyer, published at Frankfort, in 1682, and a good summary of this work is given in No. 21.

The publishers of the *Memorials* did not hesitate to include abstracts of their own publications, such as the celebrated John Ray's *Methodus Plantarum nova* (24) and the little classic on

[1] P. Johnston-Saint: "The First English Medical Journal," *Med. Press and Circ.*, 1939, **201**, 117. Douglas Guthrie: *A History of Medicine*, 1945, p. 192. London: Nelson.

[2] *Bull. Hist. Med.*, 1934, **2**, 285.

[3] This claim has been challenged by Eugène Guitard in his book *Deux Siècles de Presse au Service de la Pharmacie* (Paris, 1913). He gives priority to the *Mémoires concernant les Arts et les Sciences* of J. B. Denis (1672), thus offering a curious parallel to the claims made in this article for the *Weekly Memorials*.

brain surgery by the Plymouth surgeon James Yonge (29). The interest and importance of the matter in any abstract journal always depend upon the quality of original work available at a particular time, and in this respect the year 1682 seems to have been a fortunate one. In the latter half of the year the names of J. C. Peyer ("Peyer's patches") and J. C. Brunner ("Brunner's glands") figure prominently in the *Memorials*. Peyer's *Parerga Anatomica et Medica Septem* (Amsterdam, 1681–2) is noticed at length in Nos. 30 and 32; and the account of Brunner's *Experimenta nova circa Pancreas* occupies more than two-thirds of No. 37. Among other outstanding medical writers represented in the later numbers are J. J. van Meekeren, who was the first to record a bone-graft operation in 1668 and whose collected surgical observations, published at Amsterdam in 1682, are described in No. 43. High praise is given to the work of the celebrated Swiss physician Théophile Bonet, and the account of his *Mercurius Compitalitius, sive Index Medico-practicus*, a forerunner of our modern "systems of treatment," closes with the suggestion that anyone who translated and published an English edition "would do one of the best Pieces of Publick Service that ever has been perform'd in any Age; and next to the most Indefatigable and Learned Author himself, would deserve a *Statue* in all the *Anatomical Theatres*." The influence of the *Weekly Memorials* and the stimulus which it gave to English medical scholarship can be gauged from the fact that less than two years after this suggestion was made an English translation was published in a substantial folio volume by Thomas Flesher.

There is much else of medical interest to be found in these fifty numbers, but sufficient indication of the scope and value of the *Weekly Memorials* has already been given to prove that it warrants consideration as a medical journal. If general agreement is forthcoming on this point then it must in future be regarded not only as the first English abstracting journal but as the earliest in our long line of medical periodicals.

F. N. L. POYNTER,
Wellcome Historical Medical Museum.

THE QUESTION OF LAY PSYCHO-ANALYSIS

BY

EDWARD GLOVER, M.D.
Formerly Chairman of the Training Committee, British Psycho-analytical Society

The publication of a translation of Freud's essay on lay analysis could not have appeared at a more appropriate juncture,* for the nationalization of teaching hospitals and clinics under the control of the Ministry of Health will sooner or later raise in an acute form the professional status of the lay worker. For the time being apparently the London Clinic of Psycho-analysis has "opted out" of the national service—a concession that could be the more readily granted in that the demand for trained workers in psycho-analysis is notoriously in excess of the supply. The purveyors of a commodity in short supply can practically dictate terms to the consumer organization. Sooner or later, however, the position will change. Psycho-analysis will be compelled to a closer affiliation with teaching organizations, and this in turn will involve a more official scrutiny of training methods and selection of candidates than at present exists. The recognition some years ago by a B.M.A. Committee that only students trained at psycho-analytical centres should be called "psycho-analysts" arose from an investigation of the alleged dangers of psycho-analysis during which it was established that these sprang from the practice of "wild" analysis by untrained persons. But it was in no sense a binding pronouncement, and in practice meant next to nothing.

Freud's Case for Lay Analysis

The arguments in favour of lay analysis "under conditions," presented by Freud in this essay, are roughly as follows. Starting from the premise that a quack is a person who undertakes treatment without possessing the knowledge and capacity required for it, Freud pointed out that doctors themselves furnish the largest contingent of quacks in psycho-analysis. The training of medical students is almost exclusively in organic method, and the smattering of psychiatry they acquire is also non-psychological, certainly non-analytical, in tendency. Training in psycho-analysis is lengthy and could not very well be included in an undergraduate syllabus, which, incidentally, to meet psycho-analytical requirements would have to include specialized courses in anthropology, sociology, language, literature, and the like—in a word, orientation in the nature of cultural development. On the other hand, apart from the desirability of having a "fine ear" for mental processes, the essential prerequisite of practice is a thorough "training analysis." The analysed layman who has learned the delicate technique of analysis and knows how to handle "transferences" and "resistances" is, in Freud's view, "no longer a layman in the field of psycho-analysis."

He agreed, however, that diagnosis and recommendation of treatment must remain a medical responsibility and that organic emergencies arising in the course of an analysis must be referred to a medical specialist, implying thereby that the lay analyst must work under medical supervision; but he pointed out that in the matter of organic crises even the medical analyst, being debarred from physical examination of a patient in treatment, must refer the case to a colleague for an opinion. Moreover, in the field of child upbringing and education many disorders of adaptation are found where the question of medical knowledge does not arise. It would in any case be impossible to stop the activities of such pedagogic analysts.

Finally Freud maintained that psycho-analysis deserves a better fate than to be "swallowed up by medicine and to find its last resting-place in textbooks on psychiatry—under the heading 'Therapy.'" The theory of the unconscious mind "may become indispensable to all the branches of knowledge having to do with the origins and history of human culture and its great institutions." "At all events, it would be unreasonable to sacrifice all other uses to this one [the therapy of neuroses] merely because it touches the field of professional medicine."

Future Status of Psycho-analysis

Reviewing these arguments at a distance of over twenty years (the essay was originally published in 1926) it is interesting to note that Freud's uneasiness about the future status of psycho-analysis was not altogether without foundation. Partly because psychiatrists have in the meanwhile come to recognize that a knowledge of clinical psychology is essential to their work, and partly because of the fillip given to it by the second world war, psychiatry has gained a not altogether warranted prestige and authority in psychological matters. True, its tardy dalliance with the principles of psychology has since undergone a considerable regression, stimulated no doubt by experience of various electrical and drug therapies. But the authority of psychiatry in mental medicine has come to stay. This is in many ways unfortunate. Although a sound knowledge of psychiatry is essential to the understanding of early mental development, psychiatry has no prescriptive authority in general psycho-analysis. Indeed, there is considerable evidence that an absorption in clinical psychiatry dulls the "fine ear" for therapeutic processes. On the other hand, lay workers, not being registered medical students, are debarred from acquiring even that bare minimum of psychiatric experience that is obligatory in the medical curriculum.

An equally interesting development has occurred in the field of child-psychotherapy. As happened in the case of psycho-analysis of adults, the practice of child-analysis was soon bowdlerized; groups of so-called "play-therapeutists" whose technique bears a very remote resemblance to that of child-analysis have sprung up all over the place; indeed, play-therapy now receives the blessing of most directors of psychiatric centres and child-guidance clinics. Admittedly this form of treatment is carried out "under supervision;" nevertheless its official recognition indicates that psychiatrists have departed very considerably from the intransigent attitude they once adopted towards lay therapy.

Now, for all practical purposes these changes cancel each other out, leaving the issue of lay analysis very much where it

*Sigmund Freud: *The Question of Lay Analysis*. Translated by Nancy Procter-Gregg. London, Imago Publishing Co., 1947 (pp. 81; 9s.).

was. Under these circumstances the best way to clarify the situation is to list the mental disorders treatment of which should be carried out exclusively by medically qualified psychoanalysts and those in which it could be carried out without medical risk by properly trained lay analysts. We can then consider the advantages and disadvantages of a medical training and of a lay approach respectively.

Medical Analysts

In the first place it may be laid down that psycho-analysis of the psychoses, of borderline or larval psychotic conditions, of psychotic character cases, of severe cases of psychopathy, of most conversion hysterias and some of the anxiety states, of the traumatic neuroses and psychosomatic disorders, of alcoholism and drug addiction, should, either because of the medical risk involved or because of somatic complications, be carried out only by medical analysts. The analysis of most anxiety hysterias, a few conversion hysterias, most obsessional neuroses, general character difficulties (excluding schizoid and paranoid types), of sexual inhibitions and perversions, of most antisocial disorders, and of childhood disorders (excluding psychosomatic and psychotic types) could safely be conducted by lay analysts, who in any case are free to carry out pedagogic analyses and analysis of normal persons for purposes of research or training.

Diagnostic considerations and medical risks apart, the main advantage of medical training is not so much the acquiring of psychiatric knowledge, important as that is, as the development of a "sense of illness." Unfortunately this is discounted to some extent by the fact that most medical students are not psychologically minded. This, however, is no argument against the medical training of persons who are psychologically inclined and wish to practise medical psycho-analysis. That existing medical curricula are practically barren of psychological orientation is merely an indication of the urgent necessity to reform these curricula. In any case it would be quite practicable for any medical student to start training in psycho-analysis at a recognized institute as soon as he had completed the first part of his M.B.

The Lay Approach

So far the main arguments in favour of recognizing the treatment by lay analysts of mental illnesses that are not strictly "medical" are that lay analysts are not "spoiled" by organic training, that there is a shortage of medical analysts, and that by restricting practice to medically qualified persons some lay analysts of unusual capacity might be excluded. There is something to be said for the first argument. The advantage is, however, offset by the lay candidates' lack of scientific training, a fact which has led some Institutes to insist on an "equivalent" such as a degree in general psychology or a Ph.D. Unfortunately a training in normal psychology blunts the "fine ear" just as much as concentration on organic factors; and a Ph.D. is evidence of intellectual discipline only. More objectionable is the jealousy of their medical colleagues displayed by many lay analysts, who often take a pride in being more royalist than the King, regarding every cold in the head as being psychologically determined. Moreover, lay analysts tend to have a rather dim idea of professional codes.

Undoubtedly there have been a few lay analysts of outstanding capacity, but the percentage of these is not any higher than that found amongst medical analysts. The truth is that neither medical nor lay candidates conform to the standard of cultural development that is desirable for those undertaking the analysis of mental phenomena. Not, by the way, that it is any lower than the standard accepted for medical students. Nor can this situation be improved by adopting new-fangled and often ridiculous methods of selection. The most that teaching bodies can aim at is technical competence, and they are lucky if they get it. As for the shortage of medical analysts, this is a short-term argument of diminishing validity. It dates from the pioneer days when the medical profession was, almost to a man, violently antagonistic to the theories of Freud, which incidentally they had rarely read, and when some distinguished members of lay professions displayed their scientific temper and imagination by devoting themselves to the study of psychoanalysis. Being already in the middle years of life, it was not to be expected that they should spend another five or six years acquiring organic disciplines which under the then existing system of selection of cases they would not have occasion to use. But times have changed and there is not now the same reason to exempt those who would adopt unrestricted psychoanalytic practice from taking a medical qualification.

Need for a Faculty of Medical Psychology

But when all is said the facts remain that non-medical disciplines are just as essential to the study of psycho-analysis as training in organic methods and that many groups of cases can be expertly analysed with little more than an educated layman's knowledge of organic medicine. It is clear, therefore, that the problem of lay analysis can be solved only provided universities and colleges create an alternative medical course. Above all, what is needed is the development of a Faculty of Medical Psychology. By this I mean not just the appointment of Professors of Psychiatry or Directors of Psychiatric Centres qualified to prepare students for third-rate "diplomas" in psychological medicine, but a faculty having power to confer special degrees in medical psychology. It is not beyond the wit of university authorities to devise a course in psychological medicine in which training in organic disciplines would be drastically shorn of superfluous detail, which would give the student immensely more training in clinical psychology than is at present the case, and which would include chairs in anthropology, social and sexual disorders, the history of cultural development, and all those ancillary studies which are essential to psychological training. No doubt the further training of those who wished to specialize in psycho-analysis would of necessity remain in the hands of psycho-analytical institutes and clinics affiliated to the faculty. But we might as well face the fact that the field of psychological medicine is as wide as if not wider than that of organic medicine and calls for elaborate and specialized training.

This new creation would, however, leave two problems unsolved—namely, how to control methods of selection of psycho-analytical candidates, and how to ensure that they are soundly instructed in classical psycho-analysis. Existing methods of selection should certainly be scrapped: they are conspicuously unsuccessful. The new degree in medical psychology would surely suffice for this purpose. As for ways and means of ensuring that psycho-analysis is soundly taught, that is a more ticklish problem. Even in this country at the present time it has not proved possible to exclude from psychoanalytic teaching ideas and methods which would not be accepted by training institutes in other countries. Possibly a system of exchange scholarships whereby a number of candidates could be trained at centres abroad would help to correct these parochial deviations from classical analysis. But perhaps it would be enough if medical faculties ordered their own training on sound psychological lines; psycho-analytical institutes might then feel constrained to follow their example.

The Liverpool Regional Hospital Board is to be congratulated on bringing out a well-printed booklet giving preliminary information about the hospital and specialists services provided by the Board. This contains a map showing the position of all the hospitals supervised by the Board, and details are given of the 19 hospital management committees in the area. The public and the medical practitioners in the Liverpool hospital region are told that it is not the Board's intention to bring about immediate sweeping reforms; in general they may expect to obtain their hospital services after the appointed day as they did before. Useful information is included about how the admission of patients both to general and to special hospitals should be arranged, and the method of obtaining paybeds is described. Of particular value is the section on mental health services. This makes the new procedure of reception into a mental hospital appear simple. In the near future it is hoped to establish an emergency bed bureau service and to circulate among the practitioners in the area the names of those specialists who are prepared to undertake domiciliary consultations.

Correspondence

Diabetic Coma

SIR,—We have read Professor R. H. Micks's article (July 24, p. 200) on diabetic coma and there are several points on which we must disagree. It is not true that all America agrees that the giving of glucose early in diabetic coma is dangerous and prevents recovery, a point of view advocated by Dr. Root at Dr. Joslin's Clinic in Boston and supported by Professor Micks. What we are chiefly concerned with, however, is his advice to everyone, practitioners included, to give enormous frequent doses of insulin even in cases of what we call "pre-coma." We shall show that this is unnecessary and must involve the risk of grave hypoglycaemia.

Professor Micks does not give details of a single case to show how his theory works in practice, but we must quote some of his suggestions without taking them unfairly out of their context. If the patient can give "a clear account of himself" or is only "drowsy and confused" (hardly even pre-comatose), he should be given 100 units at first, which should produce "an obvious improvement" in 15 minutes. In our experience a subcutaneous injection of insulin never shows any effect in 15 minutes, even in the mildest diabetic. Again, "in an early case, if there is no obvious improvement in half an hour, give 100 units every half-hour until improvement is obvious"—i.e., probably many hundreds of units. We consider this unnecessary and dangerous.

The accompanying table shows four-hourly insulin dosage and blood sugars in three typical severe cases of pre-coma treated during the past year. In each case the patient could only be roused with difficulty and was therefore in a more advanced pre-comatose state than that suggested by Professor Micks's description quoted above. The total amounts of insulin required to remove the ketosis, control the blood sugar, and restore the patient to full consciousness were 124, 142, and 196 units respectively.

Hours	Case 1		Case 2		Case 3	
	Insulin	Blood Sugar	Insulin	Blood Sugar	Insulin	Blood Sugar
0	80	665 mg. %	60	800 mg. %	40	500 mg. %
4	12	256 "	20	572 "	40	512 "
8	12	200 "	30	500 "	32	280 "
12	12*	222 "	24	—	40	214 "
16	8	143 "	8	—	20*	125 "
20	0	106 "	0	200 "	12	145 "
24	—	—	0*	256 "	12	167 "

* Ketosis disappearing.

It is obvious that hundreds of units were unnecessary and would probably have produced grave hypoglycaemia—difficult to combat, we find, when vast depots of injected insulin still remain potent. We should add that we have not lost a case of so-called coma of this type for years.

The occasional case, now rarely seen by us, of profound coma with *circulatory collapse* is quite different, as also is our treatment of it. We give hundreds of units of insulin, but only when we find that the first big dose has had no effect in reducing the blood sugar in 4 hours, taking into account the slight blood-sugar dilution caused by liberal intravenous saline. We press these big doses rather empirically, thinking that owing to circulatory collapse most of this insulin is wasted and ineffective. Occasionally such patients die in spite of enormous doses of insulin and removal of ketosis because of failure to maintain an adequate circulation. This situation is quite different from the mild type mainly described by Professor Micks, where hundreds of units, in our opinion, are both unnecessary and dangerous.—We are, etc.,

Diabetic Department,
King's College Hospital,
London, S.E.5.

R. D. LAWRENCE.
WILFRID OAKLEY.

Use and Abuse of Tonsillectomy

SIR,—It would never do for anyone in authority to implement the opinion expressed by Dr. H. Stanley Banks at the Preventive Medicine Section of the Annual Meeting of the British Medical Association (July 17, p. 161) that the prohibition of tonsillectomy during epidemics (of poliomyelitis) is the only useful administrative measure of control (against the disease). But Dr. Banks's pronouncement is an important and a valuable one. Here is a well-known physician, a leader in his branch of medicine, who wants temporarily to stop all removal of tonsils during a time when some disease is prevalent that seems to him of greater importance. His opinion sounds like a challenge to Mr. V. E. Negus, speaking in another section on the same subject, to produce his evidence of the "various troubles caused by not doing the operation" until the epidemic is passed.

Let us see where such an order might lead us to. Poliomyelitis is not the only disease to which it might be applied. The post-tonsillectomy measles mastoid is so deadly that to take out tonsils during an epidemic of measles from a child who has not had the disease is as risky as to do so during an epidemic of poliomyelitis. Then were such an order made I should demand that it be extended to all such operations during the winter months and should have behind me the support of many leading physicians. I have applied the principle of cessation of tonsil operations during winter months and during measles epidemics for twenty years and have never seen any "trouble" arising from the delay. But if temporary cessations, seasonal and epidemiological, of tonsillectomy are much to be desired, why should not the administrative fiat be extended to the whole holocaust of tonsils that has been going on for a quarter of a century? It might be ordered that none should be removed under the age of nine, and then only for indications that could not be exceeded. No! Salutary as such orders would be in many ways, we cannot conduct the art of medicine by administrative fiats, and this part of the art must be amended by two other methods.

The first is that the profession as a whole should reconsider its approach to tonsillectomy. Practically every experienced physician in the land deprecates its excessive frequency. The Ministry of Education has, short of dictation, done all it can to limit the number arising from its school inspections. Yet still it goes on to such an extent that it can only be explained as being due to a disharmony of the human mind. Future generations will, I believe, wonder, and some may laugh, at our propensity to it, just as we do at the bleeding and purging of the end of the eighteenth and beginning of the last century.

The other is that parents should again assume the responsibility for decision that they have so long laid aside. The doctor does not order, he advises. If parents would say, "No, I will not have my child operated on until the epidemic is over (or until the winter is past)," they would find that the child is none the worse for the delay, and often that it has entirely recovered from the symptoms for which the operation was originally advised. The reassumption of their responsibility might thus lead inquiring minds to demand more from the doctors who advise this operation than they have in the past, and this in its turn might ensure the profession as a whole making that reconsideration that seems so necessary.—I am, etc.,

London, W.1. T. B. LAYTON.

Renal Complications in Diabetes Mellitus

SIR,—We would like to make a comment on the interesting article on renal complications in diabetes mellitus by Drs. W. R. Gauld, A. L. Stalker, and A. Lyall (July 24, p. 194). The authors admit, and we agree, that there is no certain way of distinguishing during life between intercapillary glomerulosclerosis and subacute nephritis (we should prefer to say Type II nephritis). Having found one case (No. 13) in which the typical lesions of Kimmelstiel and Wilson were not found at necropsy, they create a new group of three cases of "subacute nephritis" complicating diabetes, although in the other two cases there has been no necropsy evidence. The only criterion used by the authors in putting the other cases into this group seems to be the age of the patients.

It is wrong to assume that intercapillary glomerulosclerosis is only found in the elderly. In our present series of 16 cases (9 with necropsy confirmation) we have patients aged 47, 42, 31, 40, 42, 39, and 33. The first three of these have died and the characteristic lesion has been found. The 31-year-old patient had had diabetes for 21 years. Most of these cases have been seen by us through the courtesy of Professor T. H. Oliver, at whose diabetic clinic they have attended.—We are, etc.,

J. DAVSON.
ROBERT PLATT.

Manchester.

Prevention of Dust Diseases of the Lung

SIR,—Dr. Leonard W. Hearn says (July 17, p. 172) that grit and dust particles cannot be inhaled through a simple butter muslin or gauze mask and suggests that all workers under dusty conditions could be assured of protection against pneumoconiosis if they wore such a mask at work.

Mr. R. F. Hounam of the Pneumoconiosis Research Unit investigated the filter efficiency of a simple gauze and cotton wool mask that is produced commercially as a dust respirator and found the following results for coal dust clouds :

Particle Size	% of Particles Penetrating Mask
5 μ	30%
2 μ	70%
1 μ	90%
0.5 μ	95%

Since it is generally agreed that small particles, particularly those of 2 μ and under, are chiefly responsible for producing pulmonary fibrosis when inhaled, it may be concluded that simple gauze masks would be ineffective in the prevention of pneumoconiosis.

Members of the scientific staff of the Chemical Defence Experimental Establishment are at present collaborating with members of the scientific staff of the Pneumoconiosis Research Unit in the design of a simple but effective filter-pad to cover the mouth and nose which could be discarded after use for a single shift and which should be wearable without discomfort. A pilot model of this mask is nearly ready for trial. However, even if this simple mask is found to be wearable and effective in practice we should not like to suggest that its use should supplant dust suppression in the prevention of pneumoconiosis. I have recently seen a miner who developed advanced silicosis after only six years' work drilling in rock, during the whole of which period he wore a Mark IV respirator at work. This mask in the laboratory is at least 95% effective for particles above 0.2 μ, but it is clearly not always effective in use. My plea was for "*effective* action directed to prevention and aftercare" in the problem of pneumoconiosis. In such action the provision of dust respirators will only play a small part.—I am, etc.,

Pneumoconiosis Research Unit,
Llandough Hospital,
Nr. Cardiff.

C. M. FLETCHER.

SIR,—The letter written by Dr. Leonard W. Hearn (July 17, p. 172) is of very great interest to those of us who have spent many years in the mining areas and whose work has been more or less limited to the *x*-ray examination of miners' lungs. Dr. Hearn is "lost in wonder that no mention is made of the simple and sure means of prevention and protection by the use of the small pad" indicated by him. We also are lost in wonder that Dr. Hearn did not at some time or other make known many years ago this "simple and sure means" and thus have saved not only the lives of colliery workmen and the misery and anxiety connected with deaths due to dust disease, but also saved millions of pounds together with many hours of anxious work and research which have apparently been thrown down the drain by simple-minded people in the mining areas.

On whose authority does Dr. Hearn state that the muslin pad is a "simple and sure means of prevention"? We have failed to find any evidence of work which proves that there is "a simple and sure means of prevention and protection in dust diseases of the lung." No one has ever suggested that "grit can be inhaled," but we are at a loss to know exactly what he means by "dust particles," as this term is, to say the least, very indefinite.

Many years ago one of us (A. H.) carried out experiments with various types of mask, and by a mask we mean a mask, and not merely "six folds of butter muslin," and watched over several years the effect of these masks, including the Mk. IV so kindly given to him for that purpose by the late Professor David Jones, who assured him that dust particles of 5 μ or less would not pass through this latter type. The filtering properties of "six folds of butter muslin" cannot in any way be compared to the filters used in the Mk. IV mask. This tends to show that Dr. Hearn has rushed in where others fear to tread, as the results obtained, controlled by *x*-ray examination for a number of years, showed that the various masks were useless, as the usual proportion of patients still died from lung disease due to dust inhalation which was proved on post-mortem examination.

Very many years ago we stated that *x*-ray examination of all entrants to the coal-mining industry should be compulsory, and that periodic *x*-ray examinations of these men should be carried out so that on the earliest harmful evidence of pneumoconiosis the men should be given some other type of work away from all dust dangers. It would seem to us that, until the Medical Research Council or any other responsible persons publish evidence to the contrary, this is the only "simple and sure means of prevention and protection," or until the mining engineer can eliminate "dusts" from colliery workings. Masks of various types and masks of varying degrees of uselessness are to be found on the scrap heap in any mining area where dust disease is prevalent.—We are, etc.,

ARCHIBALD HARPER.
J. MANSEL MORGAN.

Ammanford, Carm.

Service Doctors in Far East

SIR,—The letter from Lieut. D. R. Morgan, R.A.M.C. (July 3, p. 54), complaining about the treatment of married non-regular officers in FARELF, is based on a misunderstanding of the regulations governing the grant of family passages. Owing to the shortage of quarters a points system was introduced, which was thought to be fair to all irrespective of age and rank. Married officers and men with the longest separation from their families were given the most points. The non-regular or National Service man with a total of two years to serve, and most likely not more than eighteen months overseas, is unlikely to acquire sufficient qualifying points. Families are not moved unless quarters are available, and unless the husband has at least one year's service to complete before being due to return to the United Kingdom. There are many regular officers who have had to serve their full term of three years overseas without acquiring sufficient points for their families to join them. There is no United Kingdom leave for any soldier during his three years' overseas duty tour, except for soldiers in Europe.

Lieut. Morgan appears to feel there is some discrimination between regulars and non-regulars, but both in estimating the points system and in the payment of local allowances and of marriage allowance National Service men and regular soldiers are on the same footing. A married officer who is not living with his wife and family cannot expect to receive local allowances at the rate of a married officer accompanied by his family, as he is already receiving marriage allowance at United Kingdom rates and is allowed overseas allowances for himself at single rates. The half-rate marriage allowance of officers under 25 is the same for both regular and non-regular and is not peculiar to FARELF; it applies everywhere.—I am, etc.,

R. EDGEWORTH-JOHNSTONE,
Major-General,
Director of Public Relations,

The War Office.

Golden Jubilee of the R.A.M.C.

SIR,—All will be gratified at the graceful acknowledgment by Major-General R. E. Barnsley (July 24, p. 223) of the decisive and successful action by the B.M.A. from 1896 to 1898, recorded in your leading article of June 26 (p. 1242), and commented on by Dr. W. C. Souter (July 10, p. 107), which resulted in the long-overdue establishment of the Army Medical Corps. As an addendum I would, however, remind him that no account of the detail of this outstanding piece of work can be considered complete if it omits honourable mention of the

work of the late Dr. W. Gordon, of Exeter, who at that time was secretary of the South-Western Branch of the Association. Such was the strong line he took within the Parliamentary Bills Committee on the subject of reform of the Army Medical Service that a special subcommittee was formed; and a letter from him as chairman of this subcommittee was addressed to the Secretary of State for War (Lord Lansdowne), afterwards published.[1] Later in 1896 "the elaborate and able memorandum" on the subject by the subcommittee's chairman is referred to in the proceedings of the Parliamentary Bills Committee.[2] and the report itself was published.[3] Eventually, early in 1898, a highly authoritative deputation was well received by Lord Lansdowne.[4]

It is of course not recorded in the minutes, but it is within my knowledge privately from Dr. Gordon, that Lord Lansdowne, before coming to his final and favourable conclusion, sought a further interview (which was a prolonged one) with Dr. Gordon as chairman of the subcommittee. Such ability and energy had he exhibited in the conduct of this matter that at the succeeding Annual Meeting he was awarded the thanks of the whole Association on the success of his efforts. It is appropriate that at this moment these facts be again put on record, but a full account will be found in the B.M.A.'s *Annual Handbook* of 1921–2, which contains a special historical section, and in E. Muirhead Little's *History of the B.M.A.*, p. 153, *et seq.*—I am, etc.,

Newquay, Cornwall. F. A. ROPER.

REFERENCES

1 *British Medical Journal*, 1896, **2**, 208.
2 Ibid., 1896, **2**, 1331.
3 Ibid., 1897, **1**, 732.
4 Ibid., 1898, **1**, 329.

Lower-segment Caesarean Section

SIR,—As the author, in 1933, of the use of Willett's forceps in lower-segment caesarean section I must strongly demur to Professor F. J. Browne's condemnation of them (July 10, p. 105). I have so employed them for the last 16 years and have never occasioned injury to the child's scalp beyond, in about one case in three, a small swelling underneath it, which is almost certainly mostly serum, for there is rarely any bruising, and which disappears in a week or two. They were not advocated for violent traction on the head, but only a pulling sufficient to keep it against the uterine incision and prevent bleeding from its edges. Forceful clumsiness no doubt makes them a barbarous instrument, but the barbarity is in the operator's hands and not in the forceps. I generally have two and sometimes three on at the same time, and this diminishes the force brought to bear because it is distributed over a larger area. Meanwhile the uterine incision is enlarged until it is big enough to let the head slip out. The advantage of the forceps is that they permit of traction on the head while the uterine incision is still small, and this much reduces the amount of bleeding. Sepsis, such as Professor Browne describes, argues a failure of aseptic technique by someone during or after the operation.—I am, etc.,

London, W.1. VICTOR BONNEY.

Whooping-cough and Measles

SIR,—There has recently been an outbreak of whooping-cough and of measles at an orphanage to which I have the honour to be medical officer. The children were isolated in two wards for the separate diseases, but five whooping-cough cases (aged 4–8, with duration of from 7–14 days' actual whooping and vomiting) subsequently developed measles in addition.

The first child so infected became acutely ill with bronchopneumonia, and to relieve the overworked staff I got him admitted to the local isolation hospital. The remaining four, after the usual few days' discomfort of measles, made uninterrupted recoveries, with this interesting difference. From the second or third days from the appearance of the rash they entirely lost their spasms, nor have they had further attacks although now up and about. The bronchopneumonia child had no spasms when in hospital, although he had been whooping and vomiting strongly before going. The whoops may have been missed in the general chest condition, but the matron was inclined to think he had "not been suffering from whooping-cough at all" until I told her about the others.

Are these five cases merely coincidences, or is there any known medical reason why an added measles should have apparently "cured" these distressing spasms so quickly? Mixed cases of this type must be rare and I do not remember one before in twenty-three years.—I am, etc.,

Malmesbury, Wilts. B. L. HODGE.

Acute Intussusception in Childhood

SIR,—Drs. Brenda Morrison and Donald Court are to be congratulated on their very interesting and instructive paper on this subject (April 24, p. 776). They have given a very full, accurate, and detailed description of the common signs and symptoms of this disease.

They found that fever was more commonly associated with intussusception than was usually believed to be the case. I believe, however, that the temperature is of no diagnostic significance. Also they found that the passage of blood per rectum was absent in 24% of their cases, and that 30% passed some blood within the first twelve hours. In my experience the passage of blood per rectum has been absent in some cases where the intussusception commenced in the terminal ileum within six to ten inches of the ileo-caecal valve, and these are the cases which soon become irreducible. With regard to the early diagnosis they stress the importance of a personal interview with the mother of the infant. Few cases would be missed if the doctor would listen carefully to the history of the child's illness as given by the mother, who is such an accurate and close observer where her infant's health is concerned. She notices the sudden onset of the illness, the pallor and sweating due to shock, the recurring spasms due to pain, and lastly, when it occurs, the passage of blood. With regard to the presence of a palpable abdominal tumour, this may be difficult to palpate, but there must be few if any cases where such a tumour cannot be palpated either with or without an anaesthetic.

With regard to treatment, the problem of reducing an intussusception is very similar to that where the reduction of a hernia is concerned, in that some reduce very readily and others soon become strangulated, and the duration of the trouble is not always the principal factor determining the possibility of reduction. Some will reduce easily after several days and others become irreducible within a few hours. It has been my experience after systematically attempting reduction of intussusceptions by hydrostatic pressure, using a column of saline or water from a height of three feet six inches, that over 60% of all cases presenting themselves for treatment become reduced if the pressure is maintained for eight minutes. After using this method over the last 35 years in several hundred cases I am convinced that it should always be given a trial.

Mr. Ralph H. Gardiner (May 22, p. 999) states that he regards the method of what he calls the "use of pressure enemata" as an extremely dangerous procedure, one of his reasons being the impossibility of telling whether the intussusception has been completely reduced. I know that this is also the opinion of many other surgeons. I feel sure, however, that both Mr. Gardiner and these many others have never given this method a proper trial. The method is simple, safe, and effective in most cases, and in over 40% of all cases presenting themselves for treatment one can be quite sure that reduction has been effected, although in 18% of those reduced an operation to confirm this fact should be done. If all cases are operated upon then at least 40% will be operated upon unnecessarily.

The principal sign indicating complete reduction is distension of the abdomen when no such distension of the abdomen was present before the injection was used. The distension is due to some of the saline passing through the ileo-caecal sphincter into the small bowel. It was after using thin barium enemata many years ago to bring about reduction, and then taking an *x* ray when I observed that in many cases the opaque solution had passed into the small bowel. As this brought about an even distension of the abdomen where before the injection was given the abdomen was soft and flaccid, I came to the conclusion that it was better to use hydrostatic pressure in a room adjoining the operating theatre and with the child prepared for an operation, so that no time would be wasted if one decided that an operation was necessary. I may state that in no case since using this method over the last 35 years have I made the mistake of sending the child back to the ward as having had the intussusception reduced when such was not the case.—I am, etc.,

Sydney, Australia. P. L. HIPSLEY.

Comprehensive Child Health Service

SIR,—I was very interested to read the suggestions put forward by Dr. P. O. Crossfield (July 24, p. 227) for a comprehensive child health service. I agree with him completely in all he says, and Dr. Crossfield may be interested to learn that I am attempting as an experiment and in a very modest way to provide such a combined preventive and curative child health service such as he describes.

It is obviously illogical to have one set of doctors concerned with child health and another with child disease. If one counts up the possible number of different doctors a child may see between birth and school-leaving age it is small wonder that parents receive so much conflicting, or apparently conflicting, advice. The problem of combining the two sides of paediatrics will have to be faced soon, and at the moment all that seems to have been done is a vague suggestion that general practitioners should conduct infant welfare clinics from health centres. Will each doctor see those children registered with him or will he see those of his less enthusiastic colleagues as well? If the latter, will the doctor with whom a child is registered have no objection to his patient being seen by another doctor?

I cannot see how the general practitioner working under modern conditions can possibly have time to conduct infant welfare clinics for his babies and carry out annual routine examinations of his children, and if he keeps his practice small enough to allow for this service I would then say that he was not seeing a sufficient number of children to keep experienced.

I am watching with interest to see the effect of the National Health Service on the care of children. School clinics and children's hospital out-patient departments are said to be expecting an unprecedented rush shortly as harassed G.P.s refer children for treatment they have not time to administer themselves. If this does in fact happen, then there would be sound reason for setting up a service such as that described by Dr. Crossfield.

We shall no doubt be criticized for breaking up the concept of the family doctor and for attempting to cut out yet another section of general practice. If the paediatrician visits the children in their own homes when they are ill he will soon become aware of the child's social background just as much as though he were the mother's own medical attendant, and if he works in close co-operation with the mother's doctor, say from the same health centre, then the first criticism will no longer be valid.

Rather than this scheme should be regarded as the excision of the care of children from general practice, I prefer to regard it as an attempt to grab back to general practice the work that has been done by public health authorities, but with the difference that some general practitioners should devote themselves wholly or in considerable part to the care of children only. I thus prefer the term general practitioner paediatrician, because in my scheme he would not be a substitute for the consultant paediatrician, who would still be needed for difficult cases but much of whose work could be done by the general practitioner paediatrician with his superior experience over the ordinary doctor.

The criticisms often levelled against semi-specialism in general practice are not so relevant against paediatrics, because the narrowing influence that work with one organ, or one system of the body, may have on a man is not present. Paediatrics involves a wide field of medicine, preventive and curative, applied to a certain age group, but it is a study, nevertheless, that makes specific demands upon its devotees justifying separation from the rest of medicine.

Children have already been a cause of an unforeseen difficulty in the National Health Service, to judge from the reports of doctors who have refused to take them on. We may deplore this behaviour as unethical, but there is no doubt that children require extra care, and few in the younger age groups can go through a year without requiring several items of service. Therefore, if a scheme such as Dr. Crossfield and I have outlined is to attract adherents, it is a necessary corollary that there should be a higher capitation fee for children, not only to compensate for the extra susceptibility that children have to illness but also to pay for the purely preventive services.—I am, etc.,

Bristol, 4. NORMAN J. COOK.

SIR,—May I support and extend Dr. P. O. Crossfield's admirable suggestion (July 24, p. 227) that every community should have its community paediatrician with all the children of the area "from almost conception to 12 years" on his panel? Why stop here? It is well known that the years of adolescence have their special problems. I propose an extension of Dr. Crossfield's plan: on their twelfth birthdays let all the children be transferred to the panel of a specialist for adolescents. At 20, or earlier if events necessitate it, they should of course transfer again to the list of a specialist in all that pertains to the reproductive period. Possibly for this phase there should be one specialist for each sex. The climacteriologist and the geriatrician, assuming control in their turns, would complete the scheme.

Dr. Crossfield mentions the G.P. in passing. As my logical extension of his plan eliminates the need for G.P.s to do anything but allot patients to their age groups, they may as well be abolished altogether—and with them their crazy notions about continuity of treatment and the family as the clinical unit. "The advantages are obvious, the opportunity unique."—I am, etc.,

Cambridge. H. R. YOUNGMAN.

Globin Insulin

SIR,—The warning expressed in the leading article entitled "Modern Views on Diabetes" (July 24, p. 209) against the danger of over-simplification in the treatment of diabetes is welcome. Dr. G. M. Wauchope (p. 191) seems to advocate a single, morning dose of globin insulin because of simplicity of administration. As you point out, however, the action of a single, morning injection of globin insulin is *generally* too short to control the fasting blood sugar. This is in fact well illustrated in Case 21 in Dr. Wauchope's paper, although one must grant that she has been surprisingly fortunate with her results in others.

When insulin is required it is certainly desirable to restrict its administration to a single dose in the day whenever possible. I have almost abandoned the use of globin insulin for this purpose in the average case, as in my experience very much better control can be effected with a mixture of soluble and protamine zinc insulins. Two parts of soluble with one part of protamine zinc insulin mixed in the syringe is most generally useful, but the proportions have to be adjusted to individual requirements. Unlike Dr. Wauchope, I do not find any difficulty with this method. A few cases are encountered who cannot be controlled with a single dose and would require three or four doses of soluble insulin per day. In view of my experience of the brief action of globin insulin I have tried this insulin in a number of such cases, giving morning *and* evening injections, and have found this gives satisfactory results. But these cases are exceptional.

Your other advice, that "the carbohydrate content of the diet, however large, should be kept relatively constant," is also important if proper control is to be obtained. Yet Dr. Wauchope describes her typical case as eating "mountains" (an uncertain measure) of bread and potatoes, and she "supposes" the little child John is on a free diet. However, she seems to find some dietary instructions necessary, as serious results overtook her patient who omitted his "mid-morning lunch." A suitable insulin mixture in place of globin insulin might overcome the necessity for such additional meals.—I am, etc.,

Glasgow, C.3. IAN MURRAY.

Confidential V.D. Treatment

SIR,—For over 30 years treatment of V.D. in this country has been confidential by custom and by statute. The effect of this, together with the arrangements for free voluntary treatment and careful public education, has been excellent, as the figures of attendance at public clinics show. The certainty that confidence will be kept by all concerned in the treatment, medically and administratively, is one of the main factors in inducing the early and continued attendance of persons who have—or think they have—contracted V.D. The personal troubles and family complications of such persons are in the majority of cases acute, and the disease usually has social and moral implications which are fortunately not attached in the same degree to other diseases.

The Minister of Health has, in the course of necessary rearrangements for the working of the National Health Service Act, revoked the 1916 Public Health V.D. regulations, one clause of which made this requirement of confidence statutory.

The point to be noted is that the other guiding principles in V.D. treatment—that it shall be free, and that it shall be voluntary—which were secured under the 1916 regulations are included in the new scheme. *But the important and necessary requirement of confidence on which all British V.D. treatment has been built, and on which all public propaganda is based, is deliberately left out.* No explanation has been given, nor have any satisfactory replies to Parliamentary and other questions been received.

The Minister has stated that he hopes confidence will be maintained as before, and no doubt doctors, nurses, administrators, etc., will do everything possible to observe this as in the past; but his hopes cannot have the same power and efficacy as a legal requirement. The Amendments to the N.H.S. Act which are now being drafted will presumably rectify the omissions and ambiguities of the Act. It is to be hoped that the medical profession, and all who are concerned with the treatment of patients and administration of clinics and hospitals, will urge the Minister to restore the requirement that (to quote the 1916 revoked regulation) "all information obtained in regard to any person treated under a scheme approved in pursuance of this article shall be regarded as confidential."

The public and the medical profession are already sufficiently troubled about the incidence of V.D. Why should the Minister remove, and apparently be unwilling to restore, this essential feature of our British system of V.D. treatment, which is an encouragement to sufferers to come for help and medical care, some protection to the medical profession and administrators in their difficult tasks in this field, and is admirably suited to our British constitution and character?—I am, etc.,

KATHARINE B. HARDWICK,
General Secretary.

Association for Moral and Social Hygiene.

Colonial Medical Service

SIR,—Many correspondents from many Colonial territories have drawn attention in your columns to the shortcomings of the Colonial Medical Service. It is indeed true that the pay is meagre, the equipment and administration deplorable, and the supply of drugs and doctors pitifully inadequate. It is also true that the Service contains a number of first-class men who have made, and are making, fine contributions to scientific knowledge, and that there is a wonderfully interesting job to be done in the Colonies.

After the war a number of men joined the Service who had gained considerable experience in medicine, surgery, and administration. This transfusion of new blood should be capable of reviving the patient, but alas it seems more likely to be haemolysed into premature resignation in disgust. The Colonial Medical Service has only too often lost the services of its ablest young men, and urgent action is necessary if this process is not to be repeated on a larger scale. For this state of affairs the laziness and inefficiency of some of the senior officers in the Service must share the blame with the disregard of Colonial Governors for medical and health matters.

I therefore beg, Sir, that the B.M.A. will give a lead to those members of the Service who believe that it is better to fight for a better service from within rather than to shake the dust from their feet. I suggest that the Association should take urgent action upon the following lines:

(1) Organize all B.M.A. members in the Colonial Medical Service into a strong and active branch of the Association.

(2) Bring pressure on the British Government to set up a Royal Commission to investigate medical services in the Crown Colonies, and to recommend reforms.

(3) Bring pressure on the Government to divert a proportion of national-service doctors to the Colonies for their term of conscript service as an alternative to the armed Forces.

(4) Failing effective action by the Government within six months, the B.M.A. should set up its own committee of inquiry on the Service and decide whether Association members should be recommended to resign from the Service and be deterred from joining it.

I suggest, Sir, that with strong action on these lines we could rapidly build up a Colonial Medical Service second to none, in which it would be regarded as a privilege to serve. The matter is urgent, for even the inarticulate peoples of the Colonies are beginning to realize that they are not getting the medical services they need, and to say so in no uncertain terms.—I am, etc.,

IMPERIALIST.

Moretonhampstead, Devon.

Night Thoughts

SIR,—I forward these notes in the belief that they may be of some assistance to fellow practitioners who are engaged in general practice in the present Utopian era. At 10.45 p.m. on the third day of Utopia I was called to a lady who was violently manic and possessed of systematized delusions of persecution directed against her husband. She could not be brought under control by ordinary means and spent her time either rushing wildly round the house in search of lethal weapons with which to dispatch him or creeping stealthily round listening at keyholes.

The first telephone call I made was to a colleague, requesting him to come in order that we might certify her. The second was to the home of a local J.P., but there was no reply. The third was to the gentleman who had until July 5 acted in the capacity of the Relieving Officer, but again there was no reply. When my colleague had arrived and we had seen the patient and discussed the case we put through the fourth telephone call, this time to the local police requesting their co-operation in locating the late Relieving Officer. The police sent a car to his house and found no one at home.

Meanwhile Dr. C. rang up the Blankshire County Mental Hospital and was informed that though the patient resided in Blankshire they had no jurisdiction since July 5, and advised him to contact the Area Regional Board, the telephone number of which was not known to them. The sixth call was made to Directory Inquiries, who replied that they had a list of hospitals but no number for the Area Regional Board. The seventh call was made to the mental hospital to which the patient had been admitted previously, but they under the new scheme were not permitted to readmit her. The eighth was to the convalescent hospital to which she had previously been discharged, but no information could be obtained from there.

A police sergeant and constable then arrived to inform us of the result of their attempts to find the Relieving Officer, and when I suggested that they should assist while I tackled the patient and gave her an injection the sergeant replied that it was more than his job was worth. He did agree, however, to send a message to the County Police Headquarters asking for information. That was the ninth telephone call. It was then 3.30 a.m. and I decided that it was time something definite was done. I therefore rang the Ministry of Health and had a very pleasant conversation with the night operator there. He knew of no medical man in the building, but put me in touch with the duty officer. The duty officer agreed, when I had explained the position, that things were a bit difficult, and promised to make inquiries. County Police Headquarters then rang up to say that they had located the late Relieving Officer, who had told them it was nothing to do with him.

I was then rung up by an unknown who said he was something to do with the Board of Control and had been approached by the Ministry of Health and told to communicate with me. He apologized profusely for his inability to quote chapter and verse, owing to the fact that he had not got his files in bed with him, but assured me that it was not the Relieving Officer with whom I ought to get in touch but the Duly Authorized Officer, adding, "He is usually the man who used to be the Relieving Officer."

From him I did succeed in extracting the names of all the mental hospitals in the Region, so that my eleventh call was directed to one of these. The night porter was sympathetic but explained that it was impossible to rouse any of the doctors at that hour, and would I ring again in the morning. The twelfth was to Directory Inquiries to obtain the telephone number of another mental hospital which I was unable to find in the directory. The operator was also unable to find it.

My friend the late Relieving Officer then rang up to ask why we kept sending the police to disturb him, and didn't we know that he had retired last Friday? After pacifying him I extracted the name of the Duly Authorized Officer for the area from him, and put through my thirteenth call. The Duly Authorized Officer thought that the best thing to do would be to ring up the County Hospital at Bungwell, the telephone number of which was Pingpong 2286, and see if they would help. The fourteenth call, to Pingpong 2286, produced no reply. My fifteenth call was to Directory Inquiries, who were unable to find any mention of the County Hospital at Bungwell.

My sixteenth call, to the Duly Authorized Officer, never got through, for the local operator interrupted to say that his Aunt Agatha once went nuts and was sent to the County Hospital at Bungwell, but they called it St. Bernards. He had overheard, quite unintentionally, my chat with Directory Inquiries, and had taken the liberty of looking it up in the Directory. The number was Pingpong 2256. So my seventeenth call was to Pingpong 2256. The night porter was very kind. He explained the local arrangement of telephone lines, which was so organized that though *he* could talk to the doctor on duty, should it be necessary to rouse him, *I* could not. I thanked him politely and requested him to rouse the duty officer. This he did and the ensuing relayed conversation was incomprehensible.

My eighteenth call was to the Duly Authorized Officer, who made the suggestion that if I failed to get any satisfaction from the Mental Hospital at Hungwell, Pongping 3392, he would willingly rise from his couch and come along in person. My nineteenth call, to Pongping 3392, was most edifying. I was connected almost at once with the duty officer and poured out my tale of woe. But alas, the duty officer was deaf, and not merely deaf but had only a slight knowledge of the English language.

In disgust I put through my twentieth call, to disturb the poor Duly Authorized Officer, who, some forty minutes later, preceded by ten minutes by an ambulance with the necessary attendants, arrived in person. I looked out of the window and admired the effect of the long shadows cast by the rising sun while the Duly Authorized Officer refreshed himself with a strong whisky-and-soda; and I turned in dismay as I heard him explain to Dr. C. that he hadn't got the necessary forms. It appears that he had not yet received his supplies of these essential commodities. We therefore did what was necessary in manuscript, and saw the patient safely inside the ambulance.

And as I drove home to get a shave and a quick breakfast before starting my morning surgery I thought of the blessings bestowed upon the medical profession by Saint Aneurin Bevan, whose self-confessed aim is an eight-hour day, five-day week for doctors.—I am, etc.,

PRIVATE PRACTITIONER.

POINTS FROM LETTERS

Pain in Childbirth

Dr. J. S. LAURIE (Pontefract) writes: Certain remarks in recent correspondence on pain in childbirth prompt me to suggest one simple but effective method of dealing with one of the main aspects of the problem, namely the fear of the unknown. I am aware that my procedure is by no means unique, but equally it is not practised nearly as widely as might be. As medical officer to an ante-natal clinic I hold a short talk at three-monthly intervals and during a clinic session. It is illustrated by wall charts, blackboard diagrams, and home-made plasticine models. Every woman should have at least two opportunities to attend, and although mainly intended for primiparae I find quite a large number of multiparae interested. I describe briefly and in basic English the process and meaning of menstruation, the process of gestation, with the formation of placenta, cord, membranes, and liquor, and their function. I stress the slow process of taking up and dilatation of the cervix in labour and the importance of relaxation and calm during this phase to avoid exhaustion when effort is finally required, and I warn against horrific old wives' tales. A final word about immunization and vaccination and a warning against the use of purgatives in infants winds up a total of about twenty minutes, during which my small audience is obviously intensely interested. These talks have been going on for about two years now and the results have been most gratifying; the mothers appreciate the process of labour and really do try to co-operate, with very good results.

Vaccination

Dr. J. B. GURNEY SMITH (Epsom) writes: I was interested in Mr. W. K. Fitch's remarks on this subject (July 17, p. 177). When I served in the Royal Navy in the recent war we sometimes arrived at ports where smallpox was then prevalent. Port orders were usually received on board on our arrival to state that no naval personnel were to be allowed ashore unless they had been "successfully vaccinated." I gather by successful vaccination it was meant that the individual showed a vigorous cutaneous reaction. Surely successful vaccination should imply no reaction at all and therefore no susceptibility to the incidence of smallpox. I feel the phrase "successful vaccination" is an unfortunate one and in the same category as Mr. Fitch's remarks on "take."

Herpes Zoster and Chicken-pox

Dr. A. SCOTT SMITH (Haydon Bridge, Northumberland) writes: I recently visited three children of a family who were found to be suffering from varicella. On the following day the grandfather of the children came to see me complaining of pain in the left leg which he said was "rheumatism." On examination I found that he had a herpetic rash extending from the sciatic notch to the popliteal fossa. The grandfather lives at an isolated place about two miles from his grandchildren and is visited weekly by the father of the children. He had not seen his grandchildren during the past three months and had not been in contact with any cases of chicken-pox. Presumably the father was the "carrier." The initial pain in the leg was felt two weeks after the children developed chicken-pox. The severe post-herpetic pain responded quickly to treatment with parenteral liver extract, as first described by Dr. Hugh Dickie in the *Journal* of June 15, 1946 (p. 942), and by Dr. James Kay (July 6, 1946, p. 38).

Obituary

DAME AGNES HUNT

Dame Agnes Hunt, founder of the Shropshire Orthopaedic Hospital, which is now known as the Robert Jones and Agnes Hunt Orthopaedic Hospital, Oswestry, and of the Derwen Cripples Training College, died at her home at Baschurch, Shropshire, on Saturday, July 24, at the age of 81.

Agnes Gwendoline Hunt, one of the younger members of the large family of a Shropshire squire, Rowland Hunt, of Boreatton, was born in 1867. Though a cripple herself, she trained as a nurse in the Royal Alexandra Hospital, Rhyl, and in the Salop Infirmary. She was a district nurse for 11 years, and then in 1900 she started an open-air hospital in an old house in her native village of Baschurch. Starting with subscriptions and donations amounting to £132, she finally created not only a hospital dealing with hundreds of patients but a complete organization for the aftercare of cripples in Shropshire and the Midlands. During the 1914–18 war soldiers were taken as patients, and Dame Agnes then became commandant of the Auxiliary Orthopaedic Hospital at Baschurch.

Mr. G. R. Girdlestone writes: Dame Agnes Hunt has left this troubled world after many years of the most strenuous and beneficent activity, carried through in spite of, or perhaps because of, almost constant pain and severe disablement. About 65 years ago the family doctor had found her one morning in extreme distress after a sleepless night of pain, and miserable since it meant the loss of an eagerly anticipated picnic in the hills. With kindly insight he talked of his own experiences so that she began to share his sympathies, then wrote these lines in her birthday book:

> "Reared in suffering thou shalt know
> How to solace others' woe.
> The reward of pain doth lie
> In the gift of sympathy."

He had planted a seed which grew and bore fruit beyond all imagination, for from that day she knew her destiny. Already she had learnt to try her utmost to disregard pain, illness, or anything that might prevent her from taking part in whatever was going forward. Now she had determined to become a nurse and, a cripple herself, to help to cure other cripples. Somehow she got herself accepted for training, and somehow in the end she succeeded in spite of recurring flares of hip disease. It was a triumph of resolution against all reason. In those days the training was very arduous, with long hours and wretched living conditions. She suffered from them so much herself that she vowed, "If ever I rose to be a matron, no healthy girl should be the worse in health because of her work among the sick. This vow I kept, with the result that when the Great War broke out in 1914 I was able to face it with a staff of young, stalwart, eager girls, willing and able to give of their best."[1]

After adventurous times as a district nurse with her friend Miss Goodford she started in her own village of Baschurch on Oct. 1, 1900, what grew into the first open-air orthopaedic hospital. In 1903 she consulted Robert Jones in Liverpool, and after experiencing his surgical skill herself persuaded him to see her difficult cases, and then, to her great pride and joy, to act as surgeon to her primitive hospital. Thus were linked H. O. Thomas, Robert Jones, and Agnes Hunt, the founders of a new school of orthopaedics and of a tradition of professional skill and personal service. The present writer was privileged to work at Baschurch and to spend many a Saturday night at her cottage nearby, an interlude between strenuous days in the wards and the theatre which was lit by her fascinating talk, which ranged the world but always returned to orthopaedics with insight and intimacy.

Miss Hunt had all the best qualities of individuality, charm, wisdom, and resolution, mellowed and warmed by an underlying and delightful sense of fun. She cared intensely for everything that mattered, and her response to a suffering patient was immediate and exact. We would be having a most welcome meal at the end of a long day in the theatre, of which she had borne the brunt; then would come a call from a distant ward

[1] *This is My Life.* Agnes Hunt. Blackie. 1938.

and off she would go out into the dark with her crutches and her pain, showing with that half-smile the effort and victory of her courage. Relief and reassurance went with her to the patient, for she had mastered every detail and expedient of orthopaedic nursing; her eyes were quick to see what was wrong, and her hands put it right with the sure touch and gentle strength of the craftsman.

Thus she was able to demand from her whole team the acquisition of skill and its generous expenditure in an untiring care of each individual—a devotion not to herself but to the common aim. She got all this from everyone worth their salt; the others could, and did, go. The result was a hospital intensely alive and magnificently functional and a school of orthopaedic nursing with a superb tradition.

H. B. WILLOUGHBY SMITH, M.B., B.S., F.R.C.S.

Hugh Bernard Willoughby Smith, the eldest son of Mr. E. J. Smith, of Bridlington, Yorkshire, and nephew of Dr. F. J. Smith, whose name will be familiar to generations of London Hospital men, died on July 11 in his surgery at Gainsborough, Lincolnshire, at the age of 69. He was educated at Pocklington School and at the old Yorkshire College, which later became the University of Leeds, and at the London Hospital, being a scholar in anatomy and biology. He graduated M.B., B.S.Lond., and also took the M.R.C.S., L.R.C.P. in 1902. He then served as house-surgeon at the London Hospital and at Poplar Hospital, where he obtained a grounding in E.N.T. work. In the next three years he worked as senior medical officer at Pretoria Hospital, Transvaal, and gained considerable surgical experience. Returning to England, he took the F.R.C.S. in 1909 and shortly afterwards joined the partnership of Passmore and Lanyon in Gainsborough, both old London Hospital men, starting a career in general practice and surgery which continued to the day of his death. It was interrupted only during the first world war, when he served in the 4th Northern General Hospital at Lincoln and later in various units in France. In his first few years at Gainsborough there was no hospital, and the operations were performed on a portable table, and even on the domestic kitchen table, with the help of the district nurse and an anaesthetist armed only with open chloroform or ether. There were no fatalities, and the results were so remarkably good that Willoughby Smith had built up a considerable local reputation for himself by the time the John Coupland Hospital was opened in 1913, where all his later work was done.

In addition to his surgery and general practice Smith was for many years medical officer for the Gainsborough Rural District and an active member of the B.M.A., which he joined in 1907. He was president of the Midland Branch in 1921, chairman of the Lincoln Division in 1931–2, president of the Lincolnshire Branch in 1933–4, and representative in the Representative Body from 1928 to 1939. Outside his professional work his main interests were in natural history, especially botany and gardening, in both of which he was expert.

It is, however, as a man that he will be best remembered by those privileged to be admitted to his friendship. Sincere and loyal to a fault to his colleagues and patients, he hid a warm heart under an unemotional exterior, and it is typical of him that he mentioned only very recently that the proudest moment of his life was when he received a handshake from Lord Lister during a prize-giving ceremony at the London Hospital many years ago. We shall not see his like again in private practice. Dr. Smith leaves a widow and one daughter, to whom our sympathies are given.—G. W. J.

Dr. ALEXANDER ROBB FORREST, medical officer of health for the county borough of Barrow-in-Furness, died on June 22 at the early age of 44. He was a native of Aberdeen and was educated at Robert Gordon's Colleges. Having qualified M.P.S. at Edinburgh in 1925, he studied medicine at Aberdeen University, where he graduated M.B., Ch.B. in 1930. After graduation he held various resident posts in hospitals in London and Aberdeen. In 1933 Dr. Forrest took the D.P.H. and became senior resident surgeon of Aberdeen Royal Infirmary, which post he held until the following year, when he went into general practice in Peterhead, Aberdeenshire. His duties there included those of medical officer to H.M. Prison. Three years later he gave up his practice to become assistant medical officer of health for Barrow-in-Furness, where he had clinical charge of the school medical service and children's clinics. In this particular sphere of public health work Dr. Forrest was outstandingly successful, and this was in no small measure responsible for his appointment two years later as medical officer of health and school medical officer. He thus achieved the distinction of becoming head of a department without previous experience as a deputy.

During the next few years his responsibilities were heavy indeed, for in addition to the complete reorganization of the school and welfare clinics he was called upon to organize and operate the first-aid and emergency services required for civil defence. In 1944 his thesis, "An investigation of the effect of diet and open-air methods on the physical condition of children attending an open-air school," gained for him the M.D. of Aberdeen University. Although Dr. Forrest had not enjoyed the best of health for some years, his devotion to duty was unflinching, and his enthusiasm gained the admiration and respect of all who came in contact with him. Shortly before his death he was appointed a member of the local hospital management committee and had accepted the interim post of acting secretary to that body. He was also an active member of the British Medical Association, and during the term 1946–7 was chairman of the Furness Division.

Dr. Forrest's interests outside his profession were wide, and included membership of the Barrow Rotary Club, the St. Andrew's Society, and the local branch of N.A.L.G.O. Not only was he popular among his colleagues but he enjoyed the esteem of a wide circle of friends in all walks of life. The people of Barrow have lost a zealous and respected medical officer of health who was ever ready to foster their well-being. Dr. Forrest leaves a widow and a son aged 13, to whom the deepest sympathy is extended.

Dr. MARTIN ALFRED COOKE, who died suddenly on June 28 at the age of 76, was educated at Weymouth College and at St. Bartholomew's Hospital, qualifying in 1895. He served in the Gloucester Volunteers as a private, and at the formation of the Territorial Army had attained the rank of captain. He became a major commanding a field ambulance in the London Mounted Brigade in 1908. In the 1914–18 war he commanded the Grove Hospital, Tooting, with the rank of lieutenant-colonel. For these services he was awarded the O.B.E. His first appointment on qualifying was as a house-surgeon at Stroud Hospital, which had been founded largely through the efforts of his father, Dr. A. Square Cooke, whom he later joined in practice in Stroud. In 1906 he moved to Upper Norwood and entered into partnership with the late Dr. William Gandy. From that time onwards one of his greatest interests was the Norwood Cottage Hospital, in the service of which he never spared himself. In his forty-two years of practice in Norwood Dr. Cooke got through a vast amount of work. He was a competent surgeon and performed many operations at the hospital. He was a keen Rotarian, a past president, and an inexhaustible worker for Rotarian ideals. Dr. Cooke was a man of great integrity. Many of his younger colleagues who were absent on service during the recent war have cause to remember his scrupulous care of their interests with gratitude and affection. He was beloved by his patients and respected by all who knew him. He is survived by a widow, a son, and a daughter.

Dr. HENRY SMITH, of Kew, Melbourne, Australia, died there suddenly on June 8. He was 83, and was educated at the medical school in Newcastle-upon-Tyne and was a graduate of Durham University, where he obtained his M.B. in 1890 and his M.D. four years later. His earlier professional life was spent in the cathedral city of Durham, where he carried on a general practice combined with a surgeoncy at the Durham County Hospital. He was also part-time M.O.H. to Brandon U.D.C. Smith always endeavoured to keep in touch with the best current work and to foster the best standards of the profession. He was regular in his attendance at the meetings of the old Northumberland and Durham Medical Society and a frequent visitor at operations in the Newcastle Royal Infirmary. He was also an active member of the British Medical Association and was chairman of the Durham Division from 1922 until shortly before he migrated to Australia some twenty years ago. He settled in Kew, and there he continued to practise until his death. Henry Smith was a tall, good-looking man who was always well dressed and an outstanding figure in any company. Always very courteous and attentive, with a quiet confident manner, he was very popular with his patients, to whose interests he was devoted. He was a staunch Churchman, and was a vestryman of Holy Trinity, Kew, when he died. He is survived by his widow and a daughter, who is also a member of the profession.—G.G.T.

Universities and Colleges

UNIVERSITY OF DUBLIN

SCHOOL OF PHYSIC, TRINITY COLLEGE

The following candidates have been approved at the examinations indicated:

M.D.—M. L. Abrahamson, D. H. A. Irwin, B. Kernoff, Ethna M. MacCarthy, B. M. O'Sullivan, R. Resnekov.

M.B., B.CH.—[3]J. E. F. Coolican, [2]J. A. Campbell, [2]A. L. Jones, [2]D. F. V. Lane, [2]H. A. Karrach, [2]A. M. Wiley, [2]M. S. O'Grady, [2]Maureen A. Byrne, H. A. R. Hanna, [2]Blanche Weekes, [2]D. T. Irwin, [2]Doris J. Black, [2]Margaret K. B. Knox, [2]Elizabeth E. Bird, R. B. Dockrell, Muriel T. McKenna, T. B. Madden, Sheila S. Hanbidge, R. F. Doyle, N. P. Browne, Edith E. Kyle, P. K. Storah, C. J. Davis, [3]G. W. Brown, P. A. Johnston.

M.B.—[3]E. A. Jackson, Winifred D. Eadie, T. M. W. Redman, W. H. Lefcovitch, J. K. McCall, T. G. Feeney, Anna E. Johnston, J. Diamond, C. Harris, Olivia M. Welsh, Sybil E. K. Oulton, I. J. Kritzinger, R. ff. Jackson, S. D. Boland.

B.CH.—[3]D. W. Kyle, [3]Ivy P. Robinson, [3]H. G. Alton, Dorothy C. Oswald, N. McN. Parkes, M. J. P. O'Brien, G. N. Constable, J. S. P. Lane, Dorothy I. Ogden, J. L. England, M. H. Fruithof, R. B. Flood, N. B. Hool, Hetty Hool, Peggy Moore.

B.A.O.—W. A. McGaw, C. J. Davis, Ivy P. Robinson.

The following diplomas have been awarded:

DIPLOMA IN GYNAECOLOGY AND OBSTETRICS.—G. P. Balouny, A. S. Choudhuri, M. Ghannam, S. Haydari, A. J. B. Paes.

The following prizes, etc., have been awarded:

Welland Prize, Sheine M. Schwartzberg. *Stewart Pre-medical Year Scholarship*, B. E. Kendall and Patricia A. Throup (to be divided equally). *Stewart First Medical Year Scholarship*, Lois R. Davidson. *Stewart Pre-medical Year Prizes*, Rosemary E. C. Earl and Sylvia L. E. Tyler. *Stewart First Medical Year Prizes*, Colette A. Barouch and Barbara W. M. Partridge. *Andrew Francis Dixon Prize*, R. Indar. *Aquilla Smith Prize*, Helen P. Manning. *Walter G. Smith Prize*, C. D. Levis. *Fitz-Patrick Scholarship*, J. A. Campbell. *Conolly Norman Medal in Mental Diseases*, Blanche Weekes.

[1]First-class honours in medicine. [2]Second-class honours in medicine. [3]Second-class honours in surgery.

UNIVERSITY OF LONDON

Edward Peter Sharpey-Schafer, M.B., B.Chir., M.R.C.P., has been appointed to the University Chair of Medicine tenable at St. Thomas's Hospital Medical School, from October 1.

The title of Professor Emeritus of Anatomy in the University has been conferred on Arthur Beeny Appleton, M.D., on his retirement from the Chair of Anatomy at St. Thomas's Hospital Medical School.

The title of Professor Emeritus of Medicine in the University has been conferred on Owen Lambert Vaughan Simpkinson de Wesselow, D.M., F.R.C.P., on his retirement from the Chair of Medicine at St. Thomas's Hospital Medical School.

The title of Professor Emeritus of Physiology in the University has been conferred on Daniel Thomas Harris, D.Sc., M.D., on his retirement from the Chair of Physiology at the London Hospital Medical College.

The title of Professor Emeritus of Anatomy in the University has been conferred on Thomas Baillie Johnston, C.B.E., M.D., on his retirement from the Chair of Anatomy at Guy's Hospital Medical School.

The degree of D.Sc. has been conferred on J. R. Busvine (Imperial College of Science and Technology).

NATIONAL UNIVERSITY OF IRELAND

UNIVERSITY COLLEGE, DUBLIN

The following medical degrees were conferred on July 10:

M.D.—D. C. Connolly, J. J. Doherty, C. K. O'Doherty, D. J. O'Kelly.

M.CH.—*Mary Campbell.

M.A.O.—G. A. Connolly, M. Soden.

M.B., B.CH., B.A.O.—Mary P. Phelan, N. V. O'Donohoe, L. G. O'Connell, *J. McGaley, J. J. Ambrose, J. M. J. Betts, Mary M. Bools, C. Brady, D. M. Brady, R. M. Brennan, Anne Buckley, Isabella P. Carey, J. F. A. Carey, D. M. Cassidy, L. J. Collins, Eithne M. Connolly, T. B. Connors, P. J. Conroy, Mary E. Conry, *J. B. Corbett, Catherine B. Corboy, Mary J. Corridan, B. J. Daly, P. F. Darcy, J. J. Deighan, Anne T. M. Delahunt, L. D. Digby, G. P. Donnelly, D. K. Dunlea, Pauline A. J. Dunn, E. F. Dunne, S. F. Durcan, D. Dwan, Mary B. Finnegan, B. Finucane, J. P. Flanagan, Alice Forristal, Evelyn M. Gallagher, J. F. Gilvarry, B. M. Greene, M. Hamill, T. M. J. Haran, Kathleen M. A. Harkins, P. Healy, M. J. Hefferman, J. J. Keane, D. P. Keenan, A. P. Kelleher, E. P. Kelly, Marion T. Kinsella, Catherine Lalor, P. H. MacAulay, J. R. T. McCormack, J. F. McCourt, D. MacDermott, Bridget M. V. McGettigan, P. M. J. McGrath, B. K. P. MacGreevey, T. J. McGuinness, W. P. McGurk, C. A. C. Madigan, J. Magnier, F. K. Mallon, *P. P. Marray, N. F. Meagher, J. Moloney, T. M. Moylett, F. Mulcahy, Rois C. Ni Dhochartaigh, J. H. O'Brien, P. M. P. O'Connor, J. O'Hanlon, *D. O'Herlihy, D. O'Keeffe, J. O'Mara, Patri ia O'Neill, J. A. O'Reilly, P. O. O'Reilly, D. J. Purcell, P. Purcell, Katharine P. Quane, R. Quinn, Nora M. Reidy, P. Rowland, Rose H. M. Shields, P. J. Stokes, Mary J. Tempany, J. A. Tyndall, E. A. Viani, Anna M. Walsh, C. Walsh, K. J. Walshe.

The following diplomas were awarded:

D.P.M.—*J. Dundas, *T. O. T. Egan, *M. J. Gilvarry, *B. J. Hand.

D.C.H.—*Deirdre M. Drew, T. P. O'Brien, *Eileen J. Owens, *Mary P. Fleming, P. J. O'Dwyer, J. J. Stack.

D.P.H.—B. A. O'Donnell, F. O'Nolan, J. P. O'Riordan, Mary A. Montgomery, *G. W. Ward, *J. L. Nolan, *M. E. Barry, *J. Reidy, J. P. Gannon, A. W. Pringle, E. P. F. Byrne, *C. Carey, *J. P. Corridon, *W. J. Cowhey, *J. P. Dodd, Ethna C. Fox, J. D. Grant, J. C. Joyce, P. Kent, C. W. L. Lloyd, C. W. E. Murphy, C. V. S. Murray, C. O'Donovan, K. J. Ryan, Nuala Tierney, R. M. C. Tyner.

* In absentia.

ROYAL COLLEGE OF SURGEONS OF ENGLAND

At a quarterly meeting of the Council held on July 8, Lord Webb-Johnson was re-elected President for the eighth year. Mr. L. E. C. Norbury and Mr. V. Zachary Cope were elected Vice-presidents.

Professors and Lecturers were appointed as follows:

Hunterian Professors.—Mr. Hamilton Bailey, one lecture on parotidectomy, indications and technique; Mr. Shafik Shalaby, one lecture on amoebic liver abscess; Mr. T. E. Cawthorne, one lecture on some observations on the pathology and surgical treatment of labyrinthine vertigo of non-infective origin; Dr. W. S. C. Copeman, one lecture on pathological anatomy of certain forms of lumbar fibrositis and the role of surgery in its treatment; Mr. R. W. Raven, one lecture on the properties and surgical problems of malignant melanoma; Mr. M. W. C. Oldfield, one lecture on advances in hare-lip and cleft palate surgery, following the treatment of 500 patients; Mr. C. H. Gray, one lecture on surgical treatment of the painful hip-joint; Mr. A. C. Kanaar, one lecture on pulmonary atelectasis; Mr. J. G. Bonnin, one lecture on diastasis of the tibio-fibular syndesmosis; Mr. D. F. E. Nash, one lecture on the development of micturition control; Mr. W. S. Lewin, one lecture on acute subdural and extradural haematoma in closed head injuries; Mr. Robert Roaf, one lecture on the treatment of residual disability following injuries of the peripheral nerves of the upper extremity; Mr. John Loewenthal, one lecture on the treatment of intractable ulceration of the leg, with special reference to streptomycin; Mr. R. A. R. Taylor, one lecture on the aetiology, pathology, diagnosis, and treatment of acute pancreatitis: a review of 110 cases.

Arris and Gale Lecturers.—Mr. R. K. Bowes, one lecture on infra-red photographic studies of the superficial veins in the female and their clinical application; Mr. R. H. Goetz, two lectures on the diagnosis and treatment of vascular diseases, with special consideration of clinical plethysmography and the surgical physiology of the autonomic nervous system.

Erasmus Wilson Demonstrators.—Mr. C. E. Shattock, two demonstrations; Mr. L. W. Proger, two demonstrations; Mr. R. M. Haines, one demonstration on tumours of the ovary; Mr. Guy Blackburn, one demonstration on diseases of the thyroid gland.

Arnott Demonstrators.—Mr. P. H. Mitchiner, two demonstrations; Mr. R. J. Last, two demonstrations; Dr. F. S. Gorrill, two demonstrations.

Diplomas of Fellowship were granted to the following successful candidates:

T. Levitt, B. E. Blair, R. Solley, R. Chignell, D. W. Lacey, L. P. Lassman, C. G. Scorer, J. E. Talbot, T. Faulkner, P. E. Rees-Davies, E. M. Elmhirst, R. R. Klein, P. B. Banaji, A. G. Riddell, D. W. Bain, E. Griffiths, J. Freeman, H. Salz, E. V. Hope, N. N. Iovetz-Tereshchenko, H. H. Nixon, J. H. C. Phillips, C. S. Savage, J. P. Turney, J. C. F. Cregan, J. P. Stephens, D. J. Tibbs, T. G. E. Loosemore, A. MacL. Macarthur, P. H. Schurr, J. N. Wilson, B. A. Ward, I. F. K. Muir, Margaret M. Mason, B. C. H. Luker, C. K. P. Menon, V. R. Thayumanaswami, E. Parry, L. B. Gottlieb, N. H. Morgan, J. J. Woodward, R. I. Cohen, C. I. Murphie, W. K. Smiley, J. B. Farquhar, A. R. Johnson, W. D. Sturrock, C. A. Brown, J. B. Kyle, W. J. Pullen, T. B. Smiley, D. H. Jenkins, C. J. Kaplan, R. Rowlandson, W. S. Wood, K. P. Bhargava, E. F. Chin, V. H. Cumberland, H. P. Dunn, K. G. Jayasekera, V. T. Pearse, S. S. Rose, M. F. Windsor, S. M. Boctor, J. A. Carr, H. C. Dales, K. R. Pai, R. I. R. Skelley, R. E. B. Tagart, K. Turnbull, E. A. Williams, D. V. Evans, A. E. Kark, Z. K. Kazi, R. Smith, J. W. Ardagh, C. R. Berkin, A. R. Makey, D. T. H. Paine, M. Paneth, P. F. Philip.

A Diploma of Membership was granted to R. H. R. Aston, of Birmingham.

Diplomas in Psychological Medicine, in Laryngology and Otology, and in Anaesthetics were granted, jointly with the Royal College of Physicians of London, to the following successful candidates:

DIPLOMA IN PSYCHOLOGICAL MEDICINE.—P. A. Adam, G. B. Barker, Catherine H. S. Begg, S. H. Bockner, D. Cappon, R. O. Cooke, J. Donnelly, Audrey L. Ferguson, Margaret W. Ferguson, G. S. Gladstone, R. S. Hodge, D. W. K. Kay, M. R. Leahy, J. F. McHarg, R. Natarajan, D. J. Petit, G. S. Prince, A. S. L. Rae, A. G. Silver, R. H. F. Smith.

DIPLOMA IN LARYNGOLOGY AND OTOLOGY.—D. J. J. Ackermann, A. C. Cox, N. S. Daw, D. A. Draffin, B. I. Eames, I. N. Fulton, H. Hazra, P. H. Huggill, M. S. Khan, R. A. Lindsay, R. L. McFadden, E. A. Malkin, M. Mohsin, A. T. P. Pitt, D. M. Stevens, J. G. Stonham.

DIPLOMA IN ANAESTHETICS.—R. I. W. Ballantine, M. M. Boyle, A. S. Brown, J. R. Espien, J. K. Farquhar, Violet Fry, A. H. Granat, D. J. Hadfield, Marie E. Hill, D. A. B. Hopkin, M. D. C. Hosford, H. Jackson, P. D. Johnson, R. H. N. Lake, H. L. Leaming, W. J. Lewis, L. H. Lithman, P. F. M. MacDonagh, A. Mackenzie, G. A. Mandow, T. Marshall, J. G. Millers, J. Moore, W. D. Munro, C. J. K. Orr, A. Owen-Flood, H. P. L. Ozorio, C. H. Podesta, E. S. Pope, T. R. Steen, M. Swerdlow, D. V. Thomas, Frances M. Uyatt, C. Umagiliya, H. Walker, Abigail T. Welsh, H. B. Young.

The following hospitals were recognized: Staincliffe County Hospital, Dewsbury (resident surgical officer); Northampton General Hospital (resident surgical officer, surgical registrar, and orthopaedic house-surgeon. Additional recognition); St. Andrew's Hospital, Dollis Hill, London, N.W. (senior and junior house-surgeons); Central Middlesex County Hospital, London, N.W. (the three house-surgeons); County Hospital, Whiston, Lancs (resident surgical officer, class III (rehabilitation) officer, and general house-surgeon).

FACULTY OF DENTAL SURGERY

The first election of Fellows to the Board of Faculty of Dental Surgery was held on July 16, when it was reported that Professor

H. F. Humphreys had been re-elected and Professors M. A. Rushton and H. H. Stones elected to the Board.

The Board welcomed members of the Orthodontic Society of Europe, who were shown the Odontological Museum by the Curator, Sir Frank Colyer, and inspected various College treasures.

The first meeting of the Faculty was held, and some 160 Fellows and Licentiates in Dental Surgery of the College attended. The President, Lord Webb-Johnson, gave a historical survey of the College and its association with dental surgery. He pointed out the great opportunity the Faculty had in promoting the art and science of dental surgery, and hoped that in the future dental surgery would look upon the College as its academic and spiritual home. The Dean then gave a short review of the various steps which led up to the forming of the Faculty and the Fellowship in Dental Surgery. The annual report of the Board, which showed that a considerable amount of work had been completed in the first year, was presented by Dr. E. W. Fish. At the conclusion of the meeting Mr. Reginald R. Course was elected to represent the Licentiates in Dental Surgery of the College on the Board.

The following dental surgeons from home and overseas were admitted by the President to the Fellowship in Dental Surgery of the College: Professor Andrew Francis Jackson, Professor Sheldon Friel, Professor J. C. Middleton Shaw, Miss K. C. Smyth, Mr. L. Russell Marsh, and Mr. B. Maxwell Stephens.

The Charles Tomes Lecture was given by Andrew Francis Jackson, D.D.S., professor of orthodontics, Temple University, Philadelphia, on "Growth and Development from the Clinical Aspect of Orthodontics."

In the evening the first anniversary dinner of the Faculty was held in the College, and was attended by some 150 dental surgeons and guests. The toast of "The College" was proposed by Professor Bradlaw, and the President, Lord Webb-Johnson, replied. Professor F. C. Wilkinson, the Vice-Dean, proposed the health of the guests, and Sir Wilson Jameson, Chief Medical Officer of the Ministry of Health, replied, and during the course of his speech referred to the important part which the Faculty would play in the future of dental surgery. The reply to the toast of the guests was also supported by Professor Jackson, who stressed the good relations which existed between this country and the United States from the academic as well as from the political point of view.

ROYAL COLLEGE OF PHYSICIANS OF IRELAND

T. St. V. W. Buss was admitted a Member of the College on July 9.

ROYAL COLLEGE OF OBSTETRICIANS AND GYNAECOLOGISTS

At a meeting of the Council of the College, held on July 24, Sir William Gilliatt was re-elected President of the College. The following officers were also re-elected: *Vice-Presidents*, Sir William Fletcher Shaw and Mr. James M. Wyatt; *Honorary Treasurer*, Mr. Arthur A. Gemmell; *Honorary Secretary*, Mr. Humphrey G. E. Arthure; *Honorary Librarian*, Mr. Frederick W. Roques; *Honorary Curator of the Museum*, Mr. Aleck W. Bourne.

The following were admitted to the Fellowship of the College: F. R. W. K. Allen, J. B. Dewar, P. J. Kearns, H. R. MacLennan, G. R. Sparrow.

The following were admitted to the Membership of the College: S. G. Aitken, I. C. Barne, W. Barr, F. Benjamin, A. B. Higginson.

The following candidates were elected to the Membership of the College: T. M. Abbas, I. S. R. Bain, Henrietta F. Banting, T. L. S. Baynes, S. Behrman, D. C. A. Bevis, C. C. Bowley, T. St. V. W. Buss, Ll. W. Cox, T. E. Elliot, P. M. Naidu, Mary E. Egerton, Margaret Fitzherbert, G. McI. Forsyth, H. D. Freeth, G. B. Gibson, J. H. Gibson, A. Graham, A. H. Grenz, Constance A. Grey, H. B. Hattam, C. C. Henneberg, E. Hesselberg, D. W. Higson, J. C. Holman, K. R. Hudson, A. G. Jones, J. B. Joyce, R. A. Irani, W. T. Kenny, G. G. Kerster, R. A. H. Kinch, S. Lask, T. L. T. Lewis, Ethna W. Little, E. L. F. McConnachie, W. Macfarlane, J. M. McKiddie, S. H. Madden, Helen M. Mayer, G. W. H. Millington, F. L. E. Musgrove, C. G. Nairn, J. R. Norris, J. J. F. O'Sullivan, J. H. Patterson, A. C. Pearson, W. H. Peek, S. D. Perchard, D. Prysor-Jones, M. S. Qureshi, E. H. Rees, S. McR. Reid, H. A. Ripman, D. N. S. Robertson, Helen M. Russell, B. W. Sanderson, H. Sayeed, S. A. Siddiki, G. A. Silley, A. A. Smith, T. Smith, G. J. Sophian, Christine M. Stacey, P. C. Steptoe, C. S. N. Swan, R. A. Thatcher, G. S. Thomas, R. G. Whitelaw, P. de S. Wijesekera, R. M. Williams, M. S. Williamson, H. G. Wolskel, P. S. Wright, R. B. Wright.

CONJOINT BOARD IN SCOTLAND

The following candidates, having passed the final examination, were admitted L.R.C.P.Ed., L.R.C.S.Ed., L.R.F.P.S.Glas., on July 28: Freda M. Addly, A. K. Bain, R. G. Blair, J. A. Brown, D. Bull, E. S. Cohen, Ruby M. Collister, Jessie McI. L. Duce, H. Fishman, A. Freedman, L. I. Freeman, D. Giannini, P. W. Grant, J. Hamilton, T. Hannah, D. P. K. Howie, N. D. Ker, A. Kilpatrick, A. Kwasnik, G. H. Lee, W. Leggat, A. J. Levine, Audrey E. Lewer, D. McN. McCurrach, A. W. D. McIntyre, Jessie K. M. Main, H. M. Marks, Catherine R. S. Mitchell, Margaret E. Morgan, A. Muir, W. W. Muir, B. Nash, Rosalie A. H. Paul, W. H. Reid, W. J. Reilly, B. Seltzer, A. E. M. Sieger, Eirlys Speck, R. K. Steen, D. F. F. Stephens, J. McC. H. Steven, J. Stewart, Gwyneth Watkins, Margaret L. Watt, Sheila M. Wheeler, G. A. Whitefield, L. Wilkie, Sophia W. Wright.

Medical Notes in Parliament

NATIONAL HEALTH SERVICE

Younger Specialists

On July 29 Sir ERNEST GRAHAM-LITTLE reported that a large class of younger specialists, including holders of grants under the various grades of the Health Scheme, had not been offered even interim contracts under the Health Service Act and were receiving approximately half the salary which they might expect from the Spens Report recommendations. He added that many of them had been qualified 10 years, were married, had families, and suffered from financial strain. Sir Ernest asked for an assurance that the adjustments would be retrospective and made quickly.

Mr. BEVAN replied that no interim contracts were necessary where, as was usual, holders of junior hospital appointments immediately before July 5 were whole-time officers, because they passed as transferred officers automatically into the employment of the appropriate hospital management committee or board of governors. Any adjustment of their present remuneration (which he knew to be often less than that recommended by the Spens Committee) must await the drawing up of agreed rates with the profession, as in the case of specialists. As soon as agreed rates were evolved he would do his best to see that retrospective adjustments from July 5 were carried out quickly.

Attendance at Confinement

Mr. PETER THORNEYCROFT inquired on July 29 whether under the National Health Service Regulations a mother was entitled to the presence of a doctor at her confinement if she desired it; or whether a doctor was entitled to decide that it was not necessary for him to attend in spite of the wish of the mother that he should do so.

Mr. BEVAN answered that a practitioner providing maternity medical services undertook to be present at the confinement if in his opinion it was required or if summoned by the midwife in attendance. In reaching his decision he would no doubt take account of the wishes of the mother.

On the same date Mr. PETER THORNEYCROFT further asked the Minister of Health whether under his regulations a mother could engage the services of a doctor privately and pay his fees for her confinement without losing the nursing and other benefits made available under the National Health Service Act.

Mr. BEVAN indicated that this was so but wished to make it clear that the woman could not pay any fees to a doctor on whose National Health Service list she was entered.

Prescribing

Sir THOMAS MOORE asked on July 29 what authority had been delegated to local medical committees to prevent a medical practitioner from prescribing any drug or medicine which he considered necessary for the treatment of an insured patient.

Mr. BEVAN wished it to be quite clear that patients were entitled to all drugs necessary for their proper treatment. Local medical committees had power only to investigate excessive prescribing.

On the same date Mr. RANDALL asked whether Mr. Bevan knew that regulations issued in connexion with the National Health Service concerning the procedure to be adopted for the investigation of excessive prescribing had created considerable feeling among the medical profession. He asked for an assurance that, while such procedure might be necessary to prevent extravagance, it would not be used to restrict the doctors.

Mr. BEVAN replied that this procedure was on similar lines to that which had been in operation for many years under the old National Health Insurance Scheme. He explained that it was aimed exclusively at extravagant prescribing and would certainly not be used to restrict any prescribing necessary for the treatment of the patient.

Mr. BEVAN said in reply to a question by Mr. HARDY that he realized how necessary it was that all the staffs concerned should understand the provisions of the National Health Service Superannuation Scheme. Officers of his Department were available to attend meetings of employees in order to explain the scheme in detail. In response to requests from employee organizations they had already attended a number of such meetings.

Assistants in N.H.S.

Sir ERNEST GRAHAM-LITTLE was assured by Mr. BEVAN on July 27 that executive councils had been asked to consent without question to the continued employment in the National Health Service of assistants employed before the appointed day. Mr. Bevan said the remuneration of such assistants was a matter for their principals, but arrangements for grants for trained assistants without previous experience were under discussion with the profession.

T.T. Milk

Mr. PIRATIN asked on July 26 to what extent T.T. milk not bottled by the farmer was subsequently kept separate and sold as T.T., and what steps Mr. Strachey took to ensure that such milk was not mixed with non-T.T. milk.

Dr. SUMMERSKILL said that in May, 1948, approximately 27% of the T.T. milk sold by producer-wholesalers in England and Wales was retailed as such. Under the Milk (Special Designations) Regulations T.T. milk sold as such must be kept separate from all other milk and sold to the consumer in sealed containers specially labelled and fitted with overlapping caps. Failure to comply with these conditions could involve dairymen in the revocation or suspension of their licences to sell T.T. milk. She regretted that only 27% was sold as T.T. milk but said that the Ministry could not govern consumer preference.

EPIDEMIOLOGICAL NOTES

Paratyphoid Outbreak

There has been an outbreak of paratyphoid B infection in Eastbourne. The first patients were admitted to hospital on July 25, and 35 suspected cases had been notified to the medical officer of health up to and including Aug. 2. On that date the source of the infection had not been traced, but investigations were being carried out with the assistance of the Public Health Laboratory Service. Since the illnesses began about the same time, it is thought that the patients, most of whom were children, may have been infected from a common source. There is no evidence at present that ice-cream was to blame.

Discussion of Table

In *England and Wales* infectious diseases were more prevalent during the week, and there were increases in the notifications of measles 622, whooping-cough 341, scarlet fever 45, acute pneumonia 37, diphtheria 33, acute poliomyelitis 13, dysentery 11.

A rise in the incidence of measles occurred in every area except in the west-midland and the south-western counties, where decreases in notifications of 146 and 54, respectively, were reported. The largest rises in the incidence of measles were in Yorkshire West Riding 285 and Yorkshire East Riding 124. The fluctuations in the local trends of whooping-cough were in general quite small, and the only large rises in notifications were in Lancashire 64 and Cheshire 55. The only variations of any size in the returns of scarlet fever were an increase of 25 in London and a decrease of 25 in Surrey. The chief features of the returns for diphtheria were rises in Durham 11 and Lancashire 8. In Lancashire 18 of the 42 cases in the county were notified in Liverpool C.B.

An increase in the notifications of dysentery from 5 to 24 was recorded in London (Hampstead 6, Kensington 6). The only other large return for dysentery was 11 in Lancashire. Acute poliomyelitis reverted to the level of a fortnight earlier. The largest numbers of notifications were Lancashire 6 (Manchester C.B. 5), London 5, Essex 4 (Saffron Walden R.D. 2), Middlesex 3, Durham 3, Wiltshire (Swindon M.B.) 2, Staffordshire 2, Yorkshire West Riding 2, Glamorganshire 2.

In *Scotland* an increase of 20 was recorded in the notifications of acute primary pneumonia. There was a decrease in the incidence of scarlet fever 41, measles 13, and dysentery 9. In contrast to the general trend a slight increase in the notifications of scarlet fever occurred in the eastern area.

In *Eire* increases were recorded with returns for whooping-cough 29 and measles 20, and decreases included diarrhoea and enteritis 16 and diphtheria 5. The largest outbreaks of whooping-cough were in Kerry (Kenmare R.D.) 25 and Donegal (Stranorlar R.D.) 15.

In *Northern Ireland* an increase of 25 occurred in the notifications of measles in Belfast C.B.

Week Ending July 24

The notifications of infectious diseases in England and Wales during the week included: scarlet fever 1,747, whooping-cough 3,359, diphtheria 139, measles 8,501, acute pneumonia 385, cerebrospinal fever 25, acute poliomyelitis 39, dysentery 108, paratyphoid 9, and typhoid 13.

No. 29

INFECTIOUS DISEASES AND VITAL STATISTICS

We print below a summary of Infectious Diseases and Vital Statistics in the British Isles during the week ended July 17.

Figures of Principal Notifiable Diseases for the week and those for the corresponding week last year, for: (a) England and Wales (London included). (b) London (administrative county). (c) Scotland. (d) Eire. (e) Northern Ireland.

Figures of Births and Deaths, and of Deaths recorded under each infectious disease, are for: (a) The 126 great towns in England and Wales (including London). (b) London (administrative county). (c) The 16 principal towns in Scotland. (d) The 13 principal towns in Eire. (e) The 10 principal towns in Northern Ireland.

A dash — denotes no cases; a blank space denotes disease not notifiable or no return available.

Disease	1948 (a)	(b)	(c)	(d)	(e)	1947 (Corresponding Week) (a)	(b)	(c)	(d)	(e)
Cerebrospinal fever	25	3	13	—	2	60	1	21	2	—
Deaths		—	—				—	—		
Diphtheria	183	18	40	14	1	202	21	27	16	5
Deaths	4	2	1	—	—	1	—	—	—	—
Dysentery	67	24	25	—	—	56	3	12	—	—
Deaths				—	—				—	—
Encephalitis lethargica, acute	1	—	—	—	—	3	—	1	—	—
Deaths		—					—			
Erysipelas			21	9	—			26	5	2
Deaths		—					—			
Infective enteritis or diarrhoea under 2 years				24					32	
Deaths	27	—	5	1	2	60	5	21	9	3
Measles*	9,459	602	70	91	78	8,400	455	50	222	8
Deaths†			—	—	1	7	—	1	1	—
Ophthalmia neonatorum	55	2	8	1	—	75	6	11	—	—
Deaths										
Paratyphoid fever	12	1	—	—	—	12	2	1 (B)	1 (B)	—
Deaths	—	—	—	—	—	—	—	—	—	—
Pneumonia, influenzal	377	19	—	2	4	306	19	2	—	3
Deaths (from influenza)‡	3	1	—	1	—	3	—	1	—	—
Pneumonia, primary			128	32				102	11	
Deaths	122	17		10	6		22		3	5
Polio-encephalitis, acute	2	—				16	2			
Deaths							—			
Poliomyelitis, acute	36	5	5	1	—	177	19	19	—	3
Deaths§	3	1					2			
Puerperal fever		—	2		—		5	9		—
Deaths										
Puerperal pyrexia‖	96	4	9	3	—	136	6	10	—	—
Deaths		—					—			
Relapsing fever	—	—			—	1	—			—
Deaths										
Scarlet fever	1,703	114	256	40	34	1,036	73	94	31	29
Deaths†			—	—	—	1	—	—	—	—
Smallpox	—	—	—	—	—	1	—	—	—	—
Deaths				—	—				—	—
Typhoid fever	4	—	—	3	—	10	—	—	5	4
Deaths	2	—	—	—	—	—	—	—	—	1
Typhus fever	—	—	—	—	—	—	—	—	—	—
Deaths				—	—				—	—
Whooping-cough*	3,416	258	18	117	10	1,931	217	40	53	4
Deaths	8	1	1	—	1	7	3	1	3	—
Deaths (0–1 year) Infant mortality rate (per 1,000 live births)	276	33	35	7	10	359	42	70	24	8
Deaths (excluding still-births)	4,090	630	507	140	104	4,149	681	581	148	111
Annual death rate (per 1,000 persons living)			10·2	8·8				12·1	9·3	
Live births	8,363	1340	915	351	253	9,687	1574	1097	396	275
Annual rate per 1,000 persons living			18·5	22·0				22·1	25·0	
Stillbirths	197	28	29			216	15	26		
Rate per 1,000 total births (including stillborn)			31					23		

* Measles and whooping-cough are not notifiable in Scotland, and the returns are therefore an approximation only.

† Deaths from measles and scarlet fever for England and Wales, London (administrative county), will no longer be published.

‡ Includes primary form for England and Wales, London (administrative county), and Northern Ireland.

§ The number of deaths from poliomyelitis and polio-encephalitis for England and Wales, London (administrative county), are combined.

‖ Includes puerperal fever for England and Wales and Eire.

Medical News

Central Health Services Council

The Minister of Health, Mr. Aneurin Bevan, has announced the members of the Central Health Services Council. It consists of 41 members, six *ex officio*. Of the other 35, one appointment is still to be made. The secretary is Mr. E. J. S. Clarke, of the Ministry of Health. The council held its first meeting on Tuesday, July 27, when Mr. Fred Messer, M.P., was elected chairman and Professor Henry Cohen vice-chairman. The full list will be published next week.

Mr. Bevan Meets Chairmen of Executive Councils

The Minister of Health met the chairmen of the 138 executive councils on July 28 for the first time to enable him to receive first-hand reports on the working of the services. The meeting also provided an opportunity for an informal exchange of views. Mr. Bevan thanked the councils for the way in which they had carried out the enormous burden of work which had fallen on them during the past few months. Reviewing the progress achieved, he said that the vast majority of doctors throughout the country were co-operating in the effort to make the new Service a success. A number of authenticated cases had, however, been brought to his notice of doctors who were discriminating in selecting patients or in the standards of amenities provided for public and private patients. He believed it was only a very small minority of doctors who were behaving in that way. He hoped that any cases which came to light would at once be investigated by the local medical committees, representing the medical profession. It was far better that the profession itself should, if possible, deal with complaints of this kind, and he felt sure that this was what the profession would wish.

New Viennese Journal of Physiotherapy

A new journal entitled *Physikalische Therapie Bäder- und Klimaheilkunde* has been started in Vienna by Springer. It is intended to discuss all aspects of physiotherapy, climatology, and balneology.

New Research Fellowships in Diabetes

The Lund Research Fellowships of the Diabetic Association have been allotted to the following:

1947–48.—Dr. J. A. L. Gilbert (full time) in the Department of Therapeutics, the Clinical Laboratory, Royal Infirmary, Edinburgh: "Problems in Diabetic Pregnancies." Dr. J. Hildes (part time) at Hammersmith Postgraduate School: "Studies in Liver Glycogen." Dr. J. A. Robertson (part time) at King's College Hospital: "Renal Complications of Diabetes."

1948–49.—Miss G. Audy (part time) in the Department of Biochemistry, University College, London: "*In vitro* Studies of Insulin Action." Mr. H. H. Fouracre Barns and Dr. M. E. Morgans (part time) at the Medical Unit, University College Hospital: "Animal Experiments in Diabetic Pregnancies." Dr. H. Harris (full time) at the Galton Laboratory, University College: "Diabetic Heredity."

The British Rorschach Forum

At a recent meeting convened by Dr. C. J. C. Earl the original Forum, which had been an informal group, was dissolved and reconstituted. The objects of the new Forum are to facilitate the exchange of views among those using the Rorschach test, to safeguard professional standards in the use of the Rorschach Method, and to encourage research among Rorschach workers. The Forum will consist of honorary fellows and members. Qualifications for future membership have been agreed and will include satisfying a selection committee of ability to use the test as a diagnostic method, as well as recognized qualifications in psychology or psychiatry, with clinical experience and experience in using the test professionally for not less than one year. The officers are Dr. C. J. C. Earl (chairman), Miss Theodora Alcock (secretary), Dr. W. Mons (treasurer). The subscription for both fellows and members is one guinea a year. Further information may be obtained from the Secretary, c/o The Tavistock Clinic, 2, Beaumont Street, London, W.1.

Register of Orthoptists

A new Register of Orthoptists has now been published by the Board of Registration of Medical Auxiliaries, and medical practitioners can obtain a copy free on application to the registrar of the board, Tavistock House North, Tavistock Square, London, W.C.1.

Wills

Mr. Philip Edward Homer Adams, of Theberton, Leiston, Suffolk, left £52,073. Surgeon Rear-Admiral Robert Harry Mornement, late R.N., of London, W.1, left £919. Dr. Percival Henderson, of Whitley Bay, Northumberland, left £9,957.

COMING EVENTS

Community Education for Mental Health

In connexion with the International Congress on Mental Health, which will be held at Central Hall, Westminster, London, S.W., from August 11 to 21, the National Association for Mental Health (39, Queen Anne Street, London, W.1) has arranged a specialist meeting on "Community Education for Mental Health" to be held at Westminster School Hall, Little Dean's Yard, London, S.W., on Friday, August 20, at 2.30 p.m. The meeting will be presided over by Dr. George S. Stevenson, medical director, National Committee for Mental Hygiene (U.S.A.), and member of the executive committee of the International Committee for Mental Hygiene. Addresses will be given by the following speakers: Dr. Doris M. Odlum (Vice-President, National Association for Mental Health), "The Future of Mental Health in England and Wales"; Dr. H. Bersot (Secretary-General, European Committee for Mental Hygiene), "Mental Health Education in Switzerland"; Miss Nina Ridenour, Ph.D. (Executive Officer, International Committee for Mental Hygiene), "Mental Health Education through the Press and Theatre, etc." The discussion following these addresses will be opened by Miss H. E. Howarth, M.A. (Tutor in Social Work, Institute of Psychiatry, London).

Congress on Population

The International Congress on Population and World Resources in Relation to the Family will be held at Cheltenham on August 23–28. The Family Planning Association has organized the Congress, which will include sessions on the following topics: world resources; essential standards of living; migration as a factor in the adjustment of national populations; sociological implications of family limitation in various typical countries; birth control as a factor in the adjustment of national population; ethical and medical advantages of planned family limitation; current and future research in problems of fertility, infertility, sex, and marriage; agencies for the dissemination of knowledge and propaganda. Group sessions will also be held to discuss improvement of international liaison, education of more primitive peoples in matters of sex, the present situation in Germany, sex education, and marriage guidance. The fee for registration, which includes provision of printed *Proceedings*, is £2, and applications should be addressed to the Cheltenham Congress Organizer, 37, Park Street, London, W.1.

APPOINTMENTS

COOKE, R. T., M.D., Pathologist to Hartlepools Hospitals Management Committee.

MANCHESTER UNIVERSITY.—The following appointments are announced: *Lecturer in Medicine*, H. T. Howat, M.B., Ch.B., M.R.C.P. *Honorary Clinical Lecturer in Medicine*, H. J. Wade, M.D., M.R.C.P. *Lecturer in Medical Neurology*, G. G. E. Smyth, M.D., F.R.C.P. *Lecturer in Otolaryngology*, H. P. Lawson, F.R.C.S.Ed., D.L.O., L.D.S. *Lecturer in Child Health*, A. Holzel, M.D., D.C.H. *Special Lecturer in Human Serology*, Fred Stratton, M.D. *Honorary Lecturer in Experimental and Radiation Therapeutics*, Harold Jackson, M.Sc., M.B., Ch.B., Ph.D. *Assistant Clinical Director of Chronic Rheumatism Research Centre*, H. S. Barber, M.D., F.R.C.P.I. *Chief Assistant in Chronic Rheumatism Research Centre*, Oscar Janus, M.B., Ch.B. *Physician in Charge of Rheumatism Research Clinic*, J. S. Lawrence, M.D.Ed., M.R.C.P. *Lecturer in Clinical Prosthetics*, A. J. Milne Gall, L.R.C.P. and L.R.C.S.Ed. *Clinical Lecturer in Surgery for Dental Students*, F. H. Scotson, F.R.C.S.

MIDDLESEX HOSPITAL, London, W.—*Assistant Physician to Department of Psychological Medicine*, J. A. Hobson, M.D., M.R.C.P., D.P.M. *Assistant Obstetric and Gynaecological Surgeon*, I. M. Jackson, F.R.C.S., M.R.C.O.G. *Anaesthetist*, A. J. H. Hewer, M.B., B.S., D.A.

SCUNTHORPE AND DISTRICT WAR MEMORIAL HOSPITAL.—*Physician*, J. H. Derek Millar, M.D., M.R.C.P. *Surgeon*, V. P. McAllister, M.Ch., F.R.C.S.Ed. *Anaesthetist*, W. N. Rollason, M.B., Ch.B., D.A. *Assistant Ear, Nose, and Throat Surgeon*, R. Morton, F.R.C.S.Ed. *Cardiologist*, J. W. Brown, M.D., F.R.C.P.

BIRTHS, MARRIAGES, AND DEATHS

BIRTHS

Hall-Smith.—On July 21, 1948, at Whitehaven, The Drive, Hove, to Dr. Angela Hall-Smith and Dr. Patrick Hall-Smith, a second son.

McAnallen.—On June 19, 1948, at St. Mary's Nursing Home, to Patricia (née Atkinson) and Dr. J. McAnallen, of 53, Watcombe Circus, Nottingham, a daughter.

Percy.—On July 23, 1948, at Birmingham Maternity Hospital, to Joyce (née Glover), wife of Dr. H. Gordon Percy, M.B.E., a daughter.

Tanner.—On July 24, 1948, to Evelyn Winifred, wife of Mr. Norman Tanner, F.R.C.S., a son.

DEATHS

Castellain.—On July 23, 1948, after a long illness, Herménégild George Pourtalès Castellain, M.D., of Moseley, Birmingham.

Dickson.—On July 25, 1948, after a short illness while at 21, Newlands Avenue, Thames Ditton, Surrey, William Arnott Dickson, M.D., F.R.C.S.Ed., M.R.C.P., D.P.H., of Parkhill, Kirkcaldy, Fife.

James.—On July 25, 1948, at Castle Hill, Fishguard, Pembrokeshire, suddenly, Thomas Hitchings James, M.R.C.S., L.R.C.P.

McIver.—On July 24, 1948 at his home in Bexhill, Sussex, Colin McIver, M.D., M.R.C.S., L.R.C.P., Lieutenant-Colonel I.M.S., retired.

Any Questions?

Correspondents should give their names and addresses (not for publication) and include all relevant details in their questions, which should be typed. We publish here a selection of those questions and answers which seem to be of general interest.

Repair of Inguinal Hernia

Q.—*What are the relative merits of whole-skin graft and the cutis graft in the repair of inguinal hernia? What is the exact technique of each, and what are their disadvantages? Are implantation dermoids and sepsis a danger in the whole-skin graft method? Is it true that the late results of fascial grafts are disappointing? If a hernia repaired with fascia has not recurred after twelve months, may one conclude that, as in ordinary repairs, the time of greatest danger is past?*

A.—It is not possible to give a short answer to this question. The following papers should be consulted: on whole-skin graft (Mair, *Brit. J. Surg.*, 1945, **32**, 381, and 1946, **34**, 42); on the cutis graft (Vihlein, A., *Arch. Surg.*, 1939, **38**, 118, and Cannaday, *Amer. J. Surg.*, 1945, **57**, 382). These references are sufficient to cover the greater part of surgical knowledge on this problem and on what is still regarded as an experimental method. The disadvantages which might be expected—sepsis and dermoid formation, for example—are not encountered in either the experimental preliminary animal operations or the clinical series in significant proportion. Later histological studies of buried skin grafts in man and animals rather tend to show a loss of epidermal elements. The late results of fascial repair are no more unsatisfactory than would be supposed in view of the unfavourable group of cases for which this method is employed. Most recurrences are within six to twelve months of operation (Edwards, H., *Brit. J. Surg.*, 1943, **31**, 172). This reference might be added as perhaps the one most generally useful and comprehensive on this point.

Synthesis of Optically Active Substances

Q.—*Is it possible to synthesize an optically active product from purely non-living materials? What is the significance of the asymmetrical carbon atom in vital processes?*

A.—Yes. It is also possible to synthesize optically active substances in which the activity is due either to an asymmetric atom other than carbon (the first such example being phenylbenzyl-allyl-methyl-ammonium iodide in 1899) or to a form of molecular dissymmetry in which there is no single asymmetric atom. A survey covering a number of such cases has been given lately by F. G. Mann (*J. R. Soc. Arts*, in press). There is little evidence on the biological significance of asymmetric carbon atoms. The case of gramicidin-S lately investigated by J. I. Harris and T. S. Work (*Nature*, 1948, **161**, 804) is, however, suggestive. Structurally, this appears to be a closed ring consisting either of five amino-acids or of the same sequence repeated before closure of the ring (Consden, Gordon, Martin, and Synge, *Biochem. J.*, 1947, **41**, 596). Four of these amino-acids are in the *l*-configuration and the fifth is in the *d* or (so-called) unnatural configuration. It has been suggested that the presence of a *d*-configuration would promote cyclization, and that it is to the latter that the antibacterial action of gramicidin-S is to be attributed. If confirmed, this would suggest further that the "unnaturalness" is not in the *d*-configuration as such but in the possibility that a mixture of *d* and *l* forms can lead to "unwanted" structures, including cyclization.

Colour of the Tongue

Q.—*Some people have a pale pink tongue, and most have a red one. Why is this? Is it of any significance?*

A.—The colour of the tongue depends on the thickness of its epithelial integument, its vascularity, and the haemoglobin content of the blood. Thus in anaemia it may appear pale pink and in polycythaemia rubra a deep purple. There is a considerable variation in normal persons in the first two properties which can account for differences in colour. Provided there is no evidence of a glossitis and there is no anaemia, differences in colour have no significance.

Care and Treatment of Nails

Q.—(*a*) *What is the explanation for the presence of the "half-moons" at the nail bases?* (*b*) *What are the causes and treatment of recurrent hangnail?* (*c*) *What general advice should be given to women in order that they may keep their nails attractive—that is, with the use of nail polish and nail polish remover, etc.—and yet healthy, with special regard to brittle nails?*

A.—(*a*) The "half-moons" deep to the proximal portions of nails correspond to the nail matrices, that specialized portion of epidermis from which the nails themselves grow. From this point they rest upon but are not in organic connexion with the nail-beds. (*b* and *c*) Hangnails are the result of trauma, rough usage, water maceration, or contact with irritants, particularly alkaline irritants. Biting and picking the nails, household chores, and manual labour may provoke the trouble. Toilet care of the nails is important: the cuticle should be gently pressed back with a towel or orange stick after washing to prevent it being drawn along the length of the nail. Regular care in this fashion from early childhood is desirable. The application of a little emollient at night is a useful prophylactic measure. Nail polish is harmless except in rare cases of idiosyncrasy, but serves no useful purpose. Preparations used to remove nail polish are harmful and should be kept off the cuticle (nail-fold) and adjacent skin. Cuticle removers are also harmful, being alkaline, and should be used sparingly and with care. Brittleness and other dystrophies of nails are almost invariably a reflection of some disturbance of general, circulatory, nervous, or emotional health and call for general treatment.

Arsenicals and Sulphonamides

Q.—*Is it safe to give an arsenical compound and a sulphonamide at the same time? In the bush, without laboratory facilities, one has often to treat cases (I refer more particularly to ophthalmic cases) which may be due either to gonorrhoea or to syphilis, or to both, and as the clinical test is wasteful of time, and may be so of drugs, I should be grateful for advice. If the risk is small, it may be justified.*

A.—There is no reason why arsenicals and sulphonamides should not be given at the same time except that both are somewhat toxic drugs: where convenient, therefore, it is just as well not to use them concurrently. The danger of giving substances containing sulphur during sulphonamide therapy has been exaggerated in the past and is little feared nowadays. When a lesion is considered to be due to syphilis or gonorrhoea or both and a definite diagnosis cannot be made, it is wise to prescribe treatment for both conditions in the interest of the patient; it is surely more economic in such circumstances to use a remedy unnecessarily than to allow the patient's possible syphilis to do irreparable damage. Penicillin, arsenic, and the sulphonamides are all comparatively cheap nowadays, and the cure of the patient is more important than the cost of remedies.

Transplantation of Ureter into Appendix

Q.—*At a bush hospital in the Congo it was necessary to perform transplantation of the ureters on seven or eight occasions because of extensive destruction of the urethra through either disease or post-partum sloughing. On two occasions the right ureter was lying in close proximity to the appendix, so it seemed natural to utilize the proximal 1/2 in. (1.25 cm.) for threading the ureter into the caecum, the left ureter being transplanted into the pelvic colon in the usual way. Both patients made good recoveries, and though there is no follow-up system, the cases being scattered over such a large area, one patient was known to be alive and leading a useful life three years after operation. Do the more fluid contents of the caecum constitute a strong contraindication for utilizing the appendix in this way?*

A.—The lower down the colon the ureter is implanted the less likelihood is there of getting reflux infection. Any surgeon who has succeeded in implanting the ureter into the appendix without ill effects, particularly while working in the Congo, is to be congratulated, but the risks are appreciable and are not to be taken if it is possible to implant the ureter at a lower level in the colon.

Recurrent Corneal Ulcers

Q.—*How should one treat recurrent corneal ulcers? What is the usual cause?*

A.—Recurrent corneal ulceration is generally the result of some endogenous disturbance. It may be part of the picture of phlyctenular ophthalmia, of acne rosacea keratitis, kerato-conjunctivitis sicca, and many other ill-defined entities. When the recurrent ulceration is confined to one eye a local factor may be responsible, such as recurrent erosion after injury, recurrent marginal ulceration in an arcus senilis, and repeated breakdown of the cornea in a degenerate eye. The first step in the management of recurrent corneal ulcer is, therefore, an accurate diagnosis, as distinct from the mere anatomical designation of recurrent corneal ulcer. Treatment will then depend on the underlying condition. The usual local treatment for corneal ulcer producing irritation of the eye is the instillation of 2 drops of 1% atropine sulphate solution two or three times a day, and the eye should be kept bandaged. The dangers of bandaging an eye if there is a mucopurulent discharge and of instilling atropine drops in the elderly must be borne in mind.

Metallic Taste

Q.—*Many patients complain of a metallic taste in the mouth—presumably a preservative. What is it, and in what food is it present?*

A.—The only obvious causes for a metallic taste in the mouth are foods treated with artificial sweetening agents such as saccharin and dulcin. Dental fillings of different metals may set up an electrolytic action in the mouth, and a metallic taste is also experienced sometimes by patients with trigeminal neuralgia. It may also form part of a neurosis, or be due to a lesion of the olfactory nerve or an irritative lesion involving the uncinate gyrus.

Early Rheumatoid Arthritis

Q.—*Can anything be done for early rheumatoid arthritis in the metacarpo-phalangeal joints? A woman aged 35 complains of pain and stiffness in these joints in each hand. Both her parents have marked rheumatoid changes in their hands. There is nothing to be made out by an examination of the patient's hands, but a radiograph discloses peri-articular decalcification with possibly slight loss of joint space and haziness of the margins, especially in the metacarpo-phalangeal joints of the index fingers. Her general health is good; she has had three children, is very active, and is of slight build. There is no known focus of sepsis or evidence of endocrine disturbance. Sedimentation rate has not been taken.*

A.—This seems to be a case of early rheumatoid arthritis, but before coming to a definite conclusion as a basis for treatment it would be important to have the sedimentation rate taken, and other more detailed investigations may be necessary In these days when women, especially housewives, are using their hands to a much greater degree than was the case before the war peri-articular fibrositis of the knuckles is not uncommon and is easily taken for true rheumatoid arthritis. It would be safe to give cod-liver oil, which seems to exert a beneficial effect in raising resistance, and guaiacol carbonate with calcium aspirin, 5 gr. (0.32 g.) of each three times a day. More specific measures—gold, vaccines, etc.—should not be undertaken without further investigation. Simple contrast baths for the hands would also help by stimulating the circulation, which is often poor in such cases. The prospect of arrest in this case seems to be good with proper treatment, but it is essential that this should be undertaken without delay.

Trophic Sores in Paraplegia

Q.—*What is the best method of treating a deep sinus of the hip region in a paraplegic patient? The sinus started as a pressure sore, which developed into a deep trophic ulcer.*

A.—The problem of long-standing trophic sores with sinuses of this type in paraplegic patients is a baffling one. It is always extremely difficult, and often impossible, both to avoid the development of such a sore and to make it heal. The main principles of treatment are to avoid further pressure on the affected area so far as possible, though this is by no means always practicable, and to maintain the area in as sterile a condition as possible by frequent attention to cleanliness and by the use of suitable local applications. The particular solution employed is not always a matter of importance, and it may be advantageous to change the nature of the local application from time to time. Solutions which are often useful include aqueous penicillin and sulphonamide preparations; acriflavine in spirit (2%); and phenoxetol, a solution of which is claimed to be effective against *Pseudomonas pyocyanea*. The flat trophic ulcer is a rather different problem: it responds very well to excision and split-skin grafting.

Visual Screening in Industry

Q.—*Of what value is the "sterosette" or "sterometer" in industrial visual screening methods? Can these instruments take the place of routine refraction in workers who are being selected for very fine work?*

A.—The "sterosette" was first introduced some years before the war. It was considered by a subcommittee of the Council of British Ophthalmologists, who decided not to recommend the use of the instrument except by ophthalmologists, since the interpretation of the results could be very variable. It was discovered that the findings might be either too harsh or too lax. There is no sure and certain method of "visual screening" except by a complete ophthalmic examination by an oculist. For example, a man may have perfect central vision with good muscular balance and stereopsis and yet be a danger to himself and his fellow-workers by reason of a defect in the field of vision. Such instruments are safe in the hands of an ophthalmologist but not in those of a nurse or technician.

NOTES AND COMMENTS

Learning to Read.—Dr. W. NICCOL (Westgate, Gloucester) writes: Among the many circumstances which may retard a child's progress in learning to read, your expert ("Any Questions?" July 3, p. 59) omits to mention congenital word-blindness, a disability known to ophthalmologists which, though it may be rare, is probably more common than is expected. It seems important that school medical officers and educationists should be aware of it. The occurrence of word-blindness as a result of cerebral disease is a long-established fact. Its occurrence as a congenital anomaly has received little attention. The child with congenital word-blindness is usually of normal intelligence; he may even excel in certain subjects—e.g., arithmetic—but he seems unable to recognize and to remember written (or printed) letters and words. He is like a child with no ear for music compelled to be a chorister. A vivid picture of congenital word-blindness has been given by Ashdown Carr (*Trans. oph. Soc.*, 1937, **57**, 579). The subject has also been dealt with by Professor Ronne (*Trans. oph. Soc.*, 1936, **56**, 331), and a sufferer from congenital word-blindness has described her personal experiences (*Brit. J. Oph.*, 1936, **20**, 73).

Treatment of Polycythaemia.—Dr. A. PINEY (London, W.) writes: The answer to the question about the treatment of polycythaemia (July 24, p. 235) is, I think, both misleading and incomplete. Thus it implies that P^{32} is, in fact, the treatment of choice, whereas it is now known that the incidence of leukaemia in cases of polycythaemia treated in this way is higher than in those treated by older methods. Again, there is no mention of the extreme discomfort of nitrogen mustard. Finally, the admirable method of treatment by bleeding and small maintenance doses of phenylhydrazine hydrochloride by mouth is ignored. This method will keep most of the patients in good health for many years; but if the slight risks of the drug are not felt to be justifiable, an equally good result is obtainable by bleeding at intervals varying from case to case.

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